

(SEQ ID NO: 1)	(SEQ ID NO: 2) (SEQ ID NO: 3) (SEQ ID NO: 4) HMG-1	ID NO: 5) HMG-2 ID NO: 7) HMG-1 ID NO: 8) HMG-1 ID NO: 9) HMG-2	NO: 11) NO: 12) NO: 13) NO: 14) NO: 15) NO: 16)	(SEQ ID NO: 169) (SEQ ID NO: 17) (SEQ ID NO: 18) (SEQ ID NO: 19) (SEQ ID NO: 20) LH-beta
N-terminus -I 01 F K G D A H T E	Trypsin peptid 02 K/R A S L A D 03 K/R T E T S S 04 K/R K L G E M	5 K/R L G E K R A 6 K/R I K S E H A G L S I G D 7 K/R A S L A D E Y E Y M R K 8 K/R I K G E H P G L S I G D 9 K/R M S E Y A F F V Q T X R	10 K/R S E H P G L S L G D T A N 11 K/R A G Y F A E X A R * 12 K/R K L E F L X A K * 13 K/R T T E M A S E Q G A 14 K/R A K E A L A A L K * 15 K/R F V L Q A K K * 16 K/R L G E M W	Protease V8 peptides -I 17 E T Q P D P G Q I L K K V P M V I G A Y T -I 18 E Y K C L K F K W F K K A T V M -I 19 E A K Y F S K X D A -I 20 E X K F Y V P -I 21 E L S F A S V R L P G C P P G V D P M V S F P V A L

									PMVIGA	TVM
•	•	YMXK	X L K	YMRK	ਲ	G A	X		ILKKV	WFKKA
	FKGDAHTE	ASLADEYE	TETSSSGL	ASLADEYE	AGYFAEXAI	TTEMASEQ	AKEALAALI	FVLQAKK	E T Q P D P G Q :	EYKCLKFKV
₹ 01	GGF-I 01	GGF-I 02	GGF-I 03		GGF-I 11	GGF-I 13	GGF-I 14	GGF-I 15	GGF-I 17	GGF-I 18

(SEQ ID NO: 19) (SEQ ID NO: 32) E K K E E /08 GGF-I 20 GGF-I 12

	Trypsin peptides	,				
GGF-II 01	K/R V H Q V W A	A K *			(SEQ ID NO: 33)	~
GGF-II 02	K/R YIFFME	PEAXS	ω Ω		(SEQ ID NO: 34)	_
GGF-II 03	K/R LGAWGP	PAFPV	. X Y		(SEQ ID NO: 35)	^
GGF-II 04	K/R WFVVIE	G K *			(SEQ ID NO: 36)	~
GGF-II 05	K/R ALAAAG	YDVEK	*	Histone H1	(SEQ ID NO: 164	4)
GGF-II 06	K/R LVLR*				(SEQ ID NO: 165	2)
GGF-II 07	K/R X X Y P G Q	NSTI		Trypsin	(SEQ ID NO: 166	(9
GGF-II 08	K/R A S P V S V G	SVQEL	V Q R *		(SEQ ID NO: 37)	_
GGF-II 09	K/R V C L L T V A	APPT			(SEQ ID NO: 38)	_
GGF-II 10	K/R D L L L X V				(SEQ ID NO: 39)	
	Ivsvl Endopentida	se-C pentio	g G			
GGF-II 11	KVHOVWAAK*	* (7.57			(SEQ ID NO: 51)	_
GGF-II 12	KASLADSGE	Y M X K*			(SEQ ID NO: 52)	_

FIG. 13
Comparison of BrdU-ELISA and [125 I]UdR Counting Method for the DNA Synthesis Assay in Schwann Cell Cultures

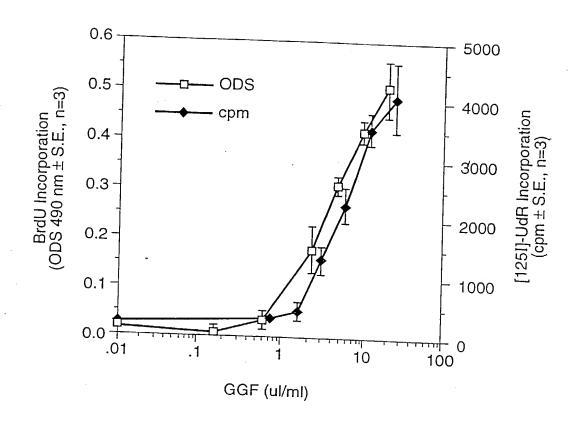


FIG. 14A
Comparison of Br-UdR Immunoreactivity
and Br-UdR Labelled Cell Number

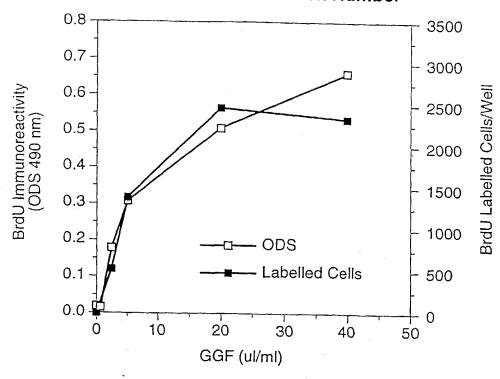


FIG. 14B
Comparison of Br-UdR Immunoreactivity
and Br-UdR Labelled Cell Number

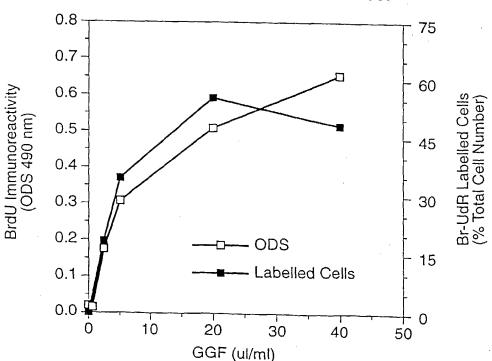


FIG. 15
Mitogenic Response of Rat Sciatic
Nerve Schwann cell to GGFs

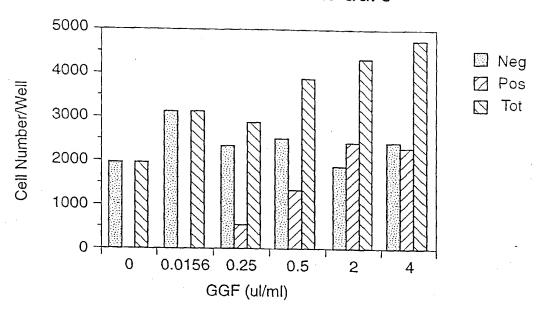


FIG. 16

DNA Synthesis in Rat Sciatic Nerve Schwann
Cells and 3T3 Fibroblasts in the presence of GGFs

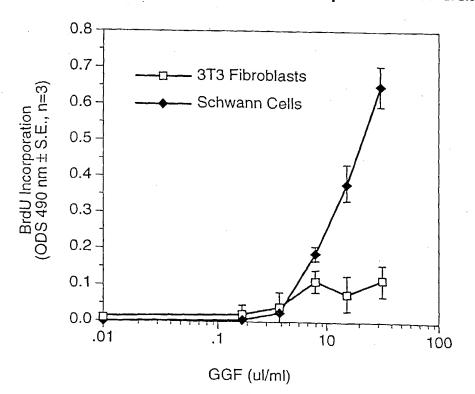


FIG. 17
Mitogenic Response of
BHK 21 C13 Cells to FCS and GGFs

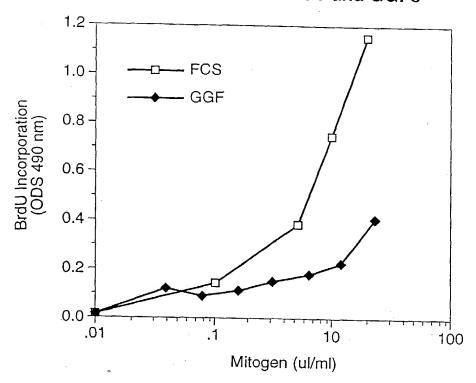


FIG. 18
Survival and Proliferation of BHK21 C13 Cell
Microcultures After 48 Hours in Presence of GGFs

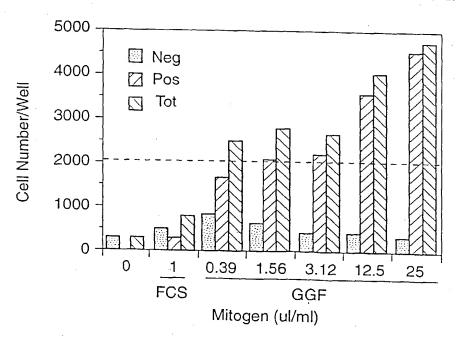


FIG. 19
Mitogenic Response of C6 Cells to FCS

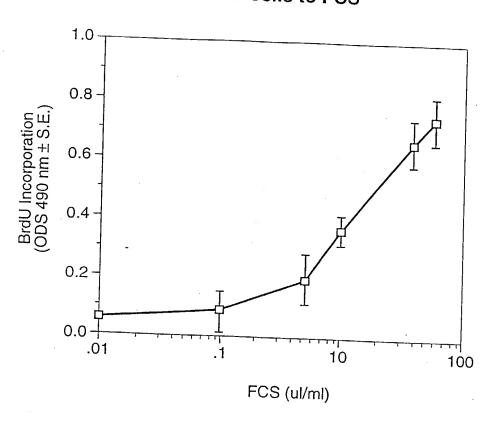


FIG. 20AMitogenic Response of C6 Cells to aFGF & GGFs

40-

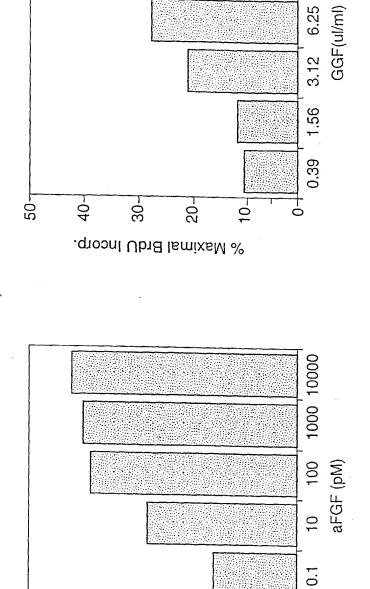
30+

% Maximal BrdU Incorp.

20-

10-

50-



12.5

0

FIG. 20B Mitogenic Response of C6 Cells to aFGF & GGFs

FIG. 21

Degenerate Oligonucleotide Probes for Factor I & Factor II

Oligo	Sequence	Peptide	
535	TTYAARGGNGAYGCNCAYAC!	GGFI-1	(CEO ID NO EA)
536	CATRTAYTCRTAYTCRTCNGC!	GGFI-2	(SEQ ID NO: 54) (SEQ ID NO: 55)
537	TGYTCNGANGCCATYTCNGT!	GGFI-13	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
538	TGYTCRCTNGCCATYTCNGT!	GGFI-13	
539	CCDATNACCATNGGNACYTT!	GGFI-17	· ·
540	GCNGCCCANACYTGRTGNAC!	GGFII-1	
541	GCYTCNGGYTCCATRAARAA!	GGFII-2	
542	CCYTCDATNACNACRAACCA!	GGFII-4	
543	TCNGCRAARTANCCNGC!	GGFI-11	
544	GCNGCNAGNGCYTCYTTNGC!	GGFI-14	·- /
545	GCNGCYAANGCYTCYTTNGC!	GGFI-14	
546	TTYTTNGCYTGNAGNACRAA!	GGFI-15	
551	TTYTTNGCYTGYAANACRAA!	GGFI-15	
568	TGNACNAGYTCYTGNAC!	GGFII-8	
569	TGNACYAAYTCYTGNAC!	GGFII-8	
609	CATRTAYTCNCCNGARTCNGC!	GGFII-12	
610	CATRTAYTCNCCRCTRTCNGC!	GGFII-12	· .
649	NGARTCNGCYAANGANGCYTT!	GGFII-12	•
650	NGARTCNGCNAGNGANGCYTT!	GGFII-12	
651	RCTRTCNGCYAANGANGCYTT!	GGFII-12	,
652	RCTRTCNGCNAGNGANGCYTT!	GGFII-12	(SEQ ID NO: 73)
653	NGARTCNGCYAARCTNGCYTT!	GGFII-12	(SEQ ID NO: 74)
654	NGARTCNGCNAGRCTNGCYTT!	GGFII-12	(SEQ ID NO: 75)
655	RCTRTCNGCYAARCTNGCYTT!	GGFII-12	(SEQ ID NO: 76) (SEQ ID NO: 78)
656	RCTRCTNGCNAGRCTNGCYTT!	GGFII-12	
659	ACNACNGARATGGCTCNNGA!	GGFI-13	(SEQ ID NO: 79) (SEO ID NO: 80)
660	ACNACNGARATGGCAGYNGA!	GGFI-13	
661	CAYCARGTNTGGGCNGCNAA!	GGFII-1	
662	TTYGTNGTNATHGARGGNAA!	GGFII-4	(SEQ ID NO: 82)
663	AARGGNGAYGCNCAYACNGA!	GGFI-1	(SEQ ID NO: 83)
664	GARGCNYTNGCNGCNYTNAA!	GGDI-14	(SEQ ID NO: 84)
665	GTNGGNTCNGTNCARGARYT!	GGFII-8	(SEQ ID NO: 85)
666	GTNGGNAGYGTNCARGARYT!	GGFII-8	(SEQ ID NO: 86)
694	NACYTTYTTNARHATYTGNCC!	GGFI-17	(SEQ ID NO: 87)
		GGL T-T1	(SEQ ID NO: 88)

FIG. 22 Putative Bovine Factor II Gene Sequences

SEQ ID NO: 89:	
TCTAA AAC TAC AGA GAC TGT ATT TTC ATG ATC ATC ATA GTT CTG TGA AAT ATA Asn Tyr Arg Asp Cys Ile Phe Met Ile Ile Ile Val Leu Xaa Asn Ile	53
CTT AAA CCG CTT TGG TCC TGA TCT TGT AGG AAG TCA GAA CTT CGC ATT Leu Lys Pro Leu Trp Ser Xaa Ser Cys Arg Lys Ser Glu Leu Arg Ile	101
AGC AAA GCG TCA CTG GCT GAT TCT GGA GAA TAT ATG TGC AAA GTG ATC Ser Lys Ala Ser Leu Ala Asp Ser Gly Glu Ser Met Cys Lys Val Ile	149
AGC AAA CTA GGA AAT GAC AGT GCC TCT GCC AAC ATC ACC ATT GTG GAG Ser Lys Leu Gly Asn Asp Ser Ala Ser Ala Asn Ile Arg Ile Val Glu	197
TCA AAC GGT AAG AGA TGC CTA CTG CGT GCT ATT TCT CAG TCT CTA AGA Ser Asn Gly Lys Arg Cys Leu Leu Arg Ala Ile Ser Gln Ser Leu Arg	245
GGA GTG ATC AAG GTA TGT GGT CAC ACT TGA ATC ACG CAG GTG TGT GAA Gly Val Ile Lys Val Cys Gly His Thr Xaa Ile Thr Gln Val Cys Glu	293
ATC TCA TTG TGA ACA AAT AAA AAT CAT GAA AGG AAA ACT CTA TGT TTG Ile Ser Cys Xaa Thr Asn Lys Asn His Glu Arg Lys Thr Leu Cys Leu	341
AAA TAT CTT ATG GGT CCT CCT GTA AAG CTC TTC ACT CCA TAA GGT GAA Lys Tyr Leu Met Gly Pro Pro Val Lys Leu Phe Thr Pro Xaa Gly Glu	389
ATA GAC CTG AAA TAT ATA TAG ATT ATT T Ile Asp Leu Lys Tyr Ile Xaa Ile Ile	417

FIG. 23APCR Primers for Factor I & Factor II

Degenerate PCR Primers

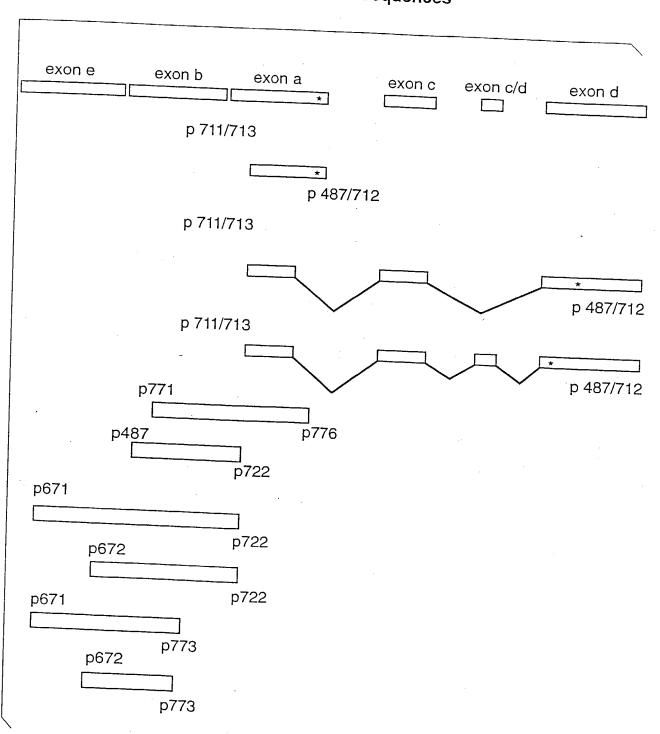
	(SEQ ID NO: 90)	(SEQ ID NO: 91)	(SEQ ID NO: 92)	(SEQ ID NO: 93)	(SEQ ID NO: 94)	(SEQ ID NO: 95)	(SEQ ID NO: 96)	(SEQ ID NO: 97)	(SEQ ID NO: 98)	(SEQ ID NO: 99)	(SEQ ID NO: 100)	(SEQ ID NO: 101)	(SEQ ID NO: 102)	(SEQ ID NO: 103)	(SEQ ID NO: 104)	(SEQ ID NO: 105)	(SEQ ID NO: 106)	(SEQ ID NO: 107)	(SEQ ID NO: 108)
Peptide	GGFI-17	GGFI-17	GGFII-12	GGFII-12	GGFII-12	GGFII-12	GGFII-1	GGFII-2	GGFII-3	GGFII-4	GGFII-1	GGFII-2	GGFII-3	GGFII-4	GGFI-2	GGFI-1	GGFI-14	GGFI-14,	GGFII-1
o Sequence	CCGAATTCTGCAGGARACNCARCCNGAYCCNGG!	AAGGATCCTGCAGNGTRTANGCNCCHATNACCATNGG!	CCGAATTCTGCAGGCNGAYTCNGGNGARTAYATG!	CCGAATTCTGCAGGCNGAYATYGGNGARTAYAT!	AAGGATCCTGCAGNNNCATRTAYTCNCCNGARTC!	AAGGATCCTGCAGNNNCATRTAYTCNCCRRTRTC!	CCGAATTCTGCAGCAYCARGTNTGGGCNGCNAA!	CCGAATTCTGCAGATRTTYTTYATGGARCCNGARG!	CCGAATTCTGCAGGGGNCCNCCNGCNTTYCCNGT!	CCGAATTCTGCAGTGGTTYGTNGTNATHGARGG!	AAGGATCCTGCAGYTTNGCNGCCCANACYTGRTG!	AAGGATCCTGCAGGCYTCNGGYTCCATRAARAA!	AAGGATCCTGCAGACNGGRAANGCNGGNGGNCC!	AAGGATCCTGCAGYTTNCCYTCDATNACNACRAAC!	CATRTAYTCRTAYTCTCNGCAAGGATCCTGCAG!	CCGAATTCTGCAGAARGGNGAYGCNCAYACNGA!	GCNGCYAANGCYRCYTTNGCAAGGATCCTGCAG!	GCNGCNAGNGCYTCYTTNGCAAGGATCCTGCAG!	TCNGCRAARTANCCNGCAAGGATCCTGCAG!
Oligo :	657	658	667	899	699	019	671	672	673	674	677	819	619	089	681	682	683	684	685

FIG. 23B PCR Primers for Factor I & Factor II

Unique PCR Primers for Factor II

Oligo	Oligo Sequence	Comment	
711	CATCGATCTGCAGGCTGATTCTGGAGAATATATGTGCA!	3' RACE	(SEQ ID NO: 109)
712	AAGGATCCTGCAGCCACATCTCGAGTCGACATCGATT!	3' RACE	(SEQ ID NO: 110)
713	CCGAATTCTGCAGTGATCAGCAAACTAGGAAATGACA!	3' RACE	(SEQ ID NO: 111)
721	CATCGATCTGCAGCCTAGTTTGCTGATCACTTTGCAC!	5' RACE	(SEQ ID NO: 112)
722	AAGGATCCTGCAGTATATTCTCCAGAATCAGCCAGTG!	5' RACE; ANCHORED	(SEQ ID NO: 113)
725	AAGGATCCTGCAGGCACGCAGTAGGCATCTTA!	EXON A	(SEQ ID NO: 114)
726	CCGAATTCTGCAGCAGAACTTCGCATTAGCAAAGC!	EXON A	(SEQ ID NO: 115)
771	CATCCCGGGATGAAGAGTCAGGAGTCTGTGGCA!	EXONS B+A	(SEQ ID NO: 116)
772	ATACCCGGGCTGCAGACAATGAGATTTCACACACCTGCG!		(SEQ ID NO: 117)
773	AAGGATCCTGCAGTTTGGAACCTGCCACAGACTCCT!	ANCHORED	(SEQ ID NO: 118)
922	ATACCCGGGCTGCAGATGAGATTTCACACACCCTGCGTGA!	EXONS B+A	(SEQ ID NO: 119)

FIG. 24
Summary of Contiguous GGF-II cDNA Structures & Sequences





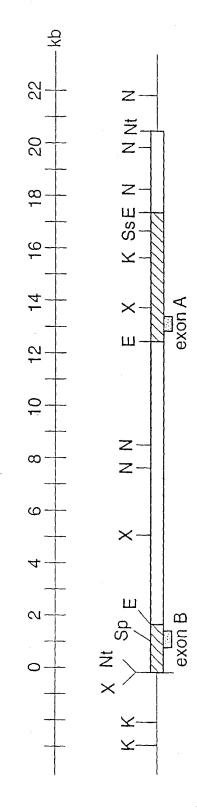


FIG. 26Alternative Gene Products of Putative Bovine GGF-II

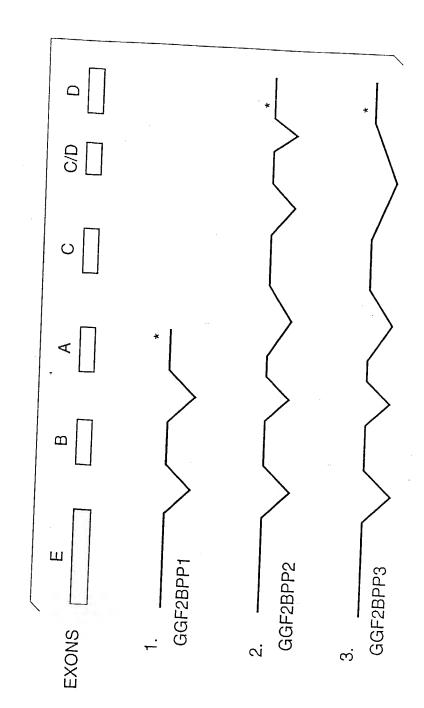


FIG. 27
GGF-II Peptides Identified in Deduced Amino Acid Sequences of Putative Bovine GGF-II Proteins

Peptide	Pos.		Sequence match	ID Sequences
II-1	1:		VHQVWAAK HQVWAAK AAGLK	(SEQ ID NO:120)
II-10	14:	GGLKK	DLLLXV dslltv RLGAW	(SEQ ID NO:121)
II-03	21:	LLTVR	LGAWGPPAFPVXY lgawghpafpscg RLKED	(SEQ ID NO:122) (SEQ ID NO:123)
II-02	41:	KEDSR	YIFFMEPEAXSSG YIFFMEPEANSSG GPGRL	(SEQ ID NO:124) (SEQ ID NO:125)
II-6	103:	VAGSK	LVLR LVLR CETSS	(SEQ ID NO:126)
I-18	112:	CETSS	EYKCLKFKWFKKATVM eysslkfkwfkngsel SRKNK	(SEQ ID NO:127) (SEQ ID NO:128)
II-12	151:	ELRIS	KASLADSGEYMXK KASLADSGEYMCK VISKL	(SEQ ID NO:129) (SEQ ID NO:130)
I-07	152:	LRISK	ASLADEYEYMRK asladsgeymck VISKL	(SEQ ID NO:131) (SEQ ID NO:132)

	55	103	151	199	247	295	343	391	439	487	535	583	625	685	44
	CTG								·	,	.,	u,		9	7
	TCG Ser														
	GAC	TGC	GAG Glu	CCC Pro	GTG Val	GAG Glu	GAA Glu	AGC	AAG Lys	\mathtt{TAT}	AAC	ATT Ile		AAGGAAAAA	rccc
	AAG Lys	TCC	CCC	CCC	GCT Ala	CAG Gln	TCT Ser	TTA Leu	GGG	GAA	GCC	GCT		AGGA?	GAGGATCCC
	AAG Lys	CCC Pro	GAG Glu	CTT Leu	$_{\rm GLY}^{\rm GGT}$	AGT	AGT Ser	GAA Glu	CCG	GGA	TCT Ser	CGT (ACT		
	TTG	TTC	ATG Met	CTC	CCG	AAG Lys	ACC Thr	AGT	AGG	TCT	GCC	ren '	CAC His '	rca T(ACTC
	GGC	GCC	TTC	AGC	CAG Gln	ATG Met	GAG Glu	GGG	AAA Lys	GAT	AGT	CTA	GGT (AAAATCATGA	GTCGACTCTA
	GGG	CCC Pro	TTC	CCG	$_{\rm G1Y}^{\rm GGT}$	GAG	TGC	AAT	CAG	GCT	GAC	TGC	TGT Cys.	1	
	GCC Ala	CAC His	ATC Ile	CTT Leu	GGA Gly	AAA Lys	CGG Arg	AAG Lys	ATA Ile	CTG . Leu	AAT	AGA Arg	GTA	TGAACAAATA	GTGGCTGCAG
	AAA Lys	GGC	TAC	CGC	GAA Glu	TTG	CTT Leu	TTC Phe	AAG Lys	TCA	GGA Gly	AAG (Lys	AAG Lys		
	GCG Ala	TGG	AGG Arg	GGC	CAA Gln	CGC Arg	GTG Val	TGG	ATC Ile	GCG Ala	CTA	GGT Gly	ATC	AATCTCATTG	GACTCGAGAT
	GCG Ala	GCC	AGC	CCC	CCT	CCC	CTA Leu	AAG Lys	AAC Asn	AAA Lys	AAA Lys	AAC Asn	GTG Val	TCTC	CTCG
	TGG Trp	GGC	GAC	GGG Gly	GAA Glu	CCT	AAA Lys	$ extstyle{TTC}$	GAA Glu	AGC	AGC Ser	TCA	GGA Gly		
	GTG Val	CTG	GAG	GGC	CCG	TTG Leu	TCC	AAG Lys	CCA Pro	ATT Ile	ATC	GAG Glu	AGA Arg	AGGTGTGTGA	AATCGATGTC
	CAA Gln	CGC	AAG Lys	AGC	$_{\rm GGG}$	GCC Ala	$_{\rm GGT}^{\rm GGT}$	CTC Leu	AAA Lys	CGC Arg	GTG Val	GTG Val	CTA	GGTG	ATCG
	CAT His	GTG Val	CTC Leu	AGC	GAC Asp	TGC	GCA Ala	TCT Ser	AAC Asn	CTT Leu	AAA Lys	ATT Ile	TCT Ser	-	
	CCTGCAG	ACC Thr	CGC Arg	AAC	CGA Arg	CGG Arg	GTG Val	TCC Ser	AAG Lys	GAA	TGC Cys	ACC	CAG Gln	TGAATCACGC	AAAAAAAAA
	CCT	CTC	GGG G1y	GCC	TCT	CAA Gln	TCT Ser	TAC	CGA Arg	TCA	ATG Met	ATC Ile	TCT Ser	TGAA	AAAA
<	⋖ 2	133:												•	
	\sim	 													
(5	2 3 1													
Ī		SEQ													

FIG. 28B

Nucleotide Sequences & Deduced Amino Acid Sequences of GGF2BPP2

SEQ ID NO: 134:

	55	103	151	199	247	295	43	161	439	487	535
	CTG Leu			. ,	. ,	(4	3	Ю	4	4	5
	TCG (Ser)						•				
	GAC :	TGC	GAG Glu	CCC Pro	GTG Val	GAG Glu	GAA Glu	AGC Ser	AAG Lys	\mathtt{TAT}	AAC
	AAG Lys	rcc Ser	CCC	CCC	GCT	CAG	TCT (Ser (TTA Z	GGG A	GAA G	GCC A
	AAG Lys	CCC Pro	GAG Glu	CTT	GGT (AGT (AGT :	GAA 5 Glu I	CCG (GGA G	TCT G
	TTG	TTC	ATG Met	CTC	CCG (Pro (AAG Z	ACC 7	AGT (AGG (Arg E	TCT G	GCC TAIA S
	GGC	GCC	TTC	AGC	CAG	ATG Met]	GAG /	GGG 7	AAA A Lys A	GAT 1 ASP 5	AGT C
	GGG G1y	CCC	TTC	CCG Pro	GGT	GAG Glu	TGC (AAT (Asn (CAG Z	GCT (Ala A	GAC A
	GCC Ala	CAC His	ATC Ile	CTT	GGA Gly	AAA Lys	CGG '	AAG Lys	ATA (Ile (CTG (Leu /	AAT (Asn A
	AAA Lys	GGC Gly	TAC	CGC	GAA Glu	TTG	CTT Leu	TTC Phe	AAG ; Lys	TCA (GGA A
	GCG Ala	TGG	AGG Arg	GGC Gly	CAA Gln	CGC	GTG	TGG '	ATC I	GCG 7	CTA (Leu (
	GCG Ala	GCC Ala	AGC Ser	CCC Pro	CCT Pro	CCC Pro	CTA	AAG Lys	AAC Asn	AAA (Lys)	AAA (Lys 1
	TGG Trp	GGC	GAC	GGG G1y	GAA Glu	CCT Pro	AAA Lys	TTC	GAA Gly	AGC . Ser]	AGC Z
	GTG Val	CTG Leu	GAG Glu	GGC Gly	CCG Pro	TTG	TCC Ser	AAG Lys	CCA (Gly (ATT Ile	ATC I
	CAA Gln	CGC Arg	AAG Lys	AGC	666 61y	GCC	$_{\rm GGT}$	CTC	AAA Lys	CGC Arg	GTG
	CAT His	GTG Val	CTC	AGC	GAC Asp	TGC	GCA Ala	TCT Ser	AAC Asn	CTT (AAA (Lys
SEX ID NO:	CCTGCAG	ACC Thr	CGC Arg	AAC Lys	CGA Arg	CGG	GTG	rcc	AAG L	GAA (Glu 1	TGC 7
S S S	CCTC	CTC	666 61y	GCC Ala	TCT	CAA Gln	TCT Ser	TAC	CGA	TCA (ATG ' Met (

FIG. 28C Nucleotide Sequences & Deduced Amino Acid Sequences of GG2BPP2

583	631	679	727	775	826	988	946	1006	1066	1126	1186	1193
ATC ACC ATT GTG GAG TCA AAC GCC ACA TCC ACA TCT ACA GCT GGG ACA Ile Thr Ile Val Glu Ser Asn Ala Thr Ser Thr Ser Thr Ala Gly Thr	AGC CAT CTT GTC AAG TGT GCA GAG AAG GAG AAA ACT TTC TGT GTG AAT Ser His Leu Val Lys Ser Ala Glu Lys Glu Lys Thr Phe Cys Val Asn	GGA GGC GAG TGC TTC ATG GTG AAA GAC CTT TCA AAT CCC TCA AGA TAC Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr	TTG TGC AAG TGC CAA CCT GGA TTC ACT GGA GCG AGA TGT ACT GAG AAT Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn	GTG CCC ATG AAA GTC CAA ACC CAA GAA AGT GCC CAA ATG AGT TTA CTG Val Pro Met Lys Val Gln Thr Gln Glu Ser Ala Gln Met Ser Leu Leu	GTG ATC GCT GCC AAA ACT ACG TAATGGCCAG CTTCTACAGT ACGTCCACTC Val Ile Ala Ala Lys Thr Thr	CCTTTCTGTC TCTGCCTGAA TAGCGCATCT CAGTCGGTGC CGCTTTCTTG TTGCCGCATC	TCCCCTCAGA TTCCTCCTAG AGCTAGATGC GTTTTACCAG GTCTAACATT GACTGCCTCT	GCCTGTCGCA TGAGAGATT AACACAAGCG ATTGTATGAC TTCCTCTGTC CGTGACTAGT	GGGCTCTGAG CTACTCGTAG GTGCGTAAGG CTCCAGTGTT TCTGAAATTG ATCTTGAATT	ACTGTGATAC GACATGATAG TCCCTCTCAC CCAGTGCAAT GAC <u>AATAAA</u> G GCCTTGAAAA	GTCAAAAAAA AAAAAAAA AAAAATCGA TGTCGACTCG AGATGTGGCT GCAGGTCGAC	TCTAGAG

FIG. 28DNucleotide Sequences & Deduced Amino Acid Sequences of GGF2BPP3

SEQ ID NO: 135:

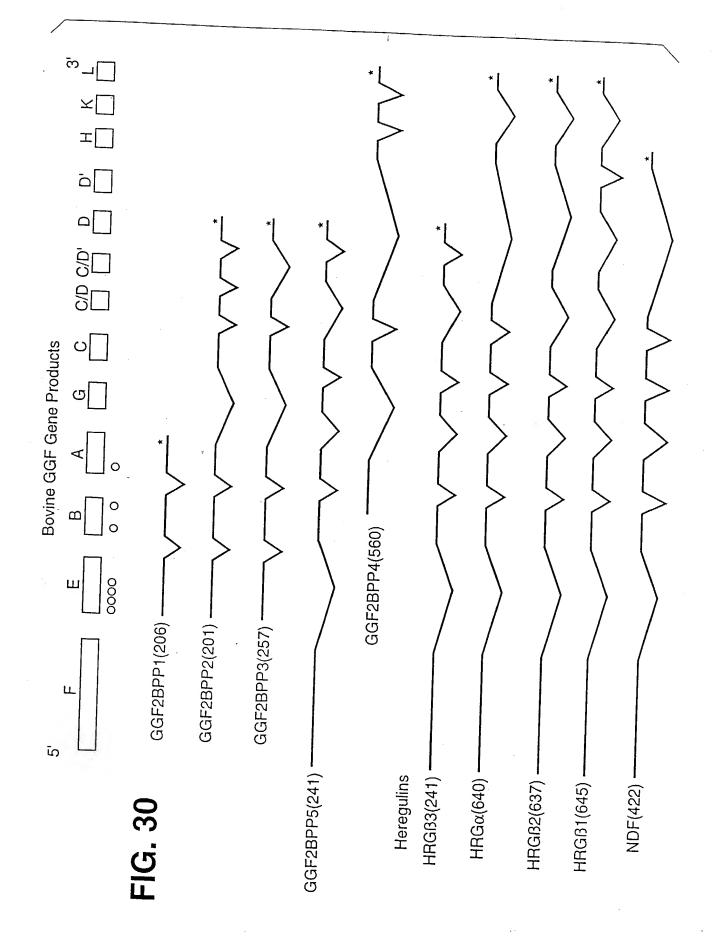
55	103	151	199	247	295	343	391	439	487
CTG Leu						. ,	, ,	7.	7.
TCG									
GAC Asp	TGC Cys	GAG Glu	CCC Pro	GTG Val	GAG	GAA Glu	AGC Ser	AAG Lys	\mathtt{TAT}
AAG Lys	TCC	CCC Pro	CCC Pro	GCT	CAG Gln	TCT Ser	TTA	GGG	GAA '
AAG Lys	CCC Pro	GAG Glu	CTT Leu	$_{\rm GLY}^{\rm GGT}$	AGT Ser	AGT Ser	GAA Glu	CCG	GGA (
TTG	TTC Phe	ATG Met	CTC	CCG	AAG Lys	ACC Thr	AGT	AGG Arg	TCT Ser
GGC	GCC Ala	TTC Phe	AGC Ser	CAG Gln	ATG Met	GAG Glu	GGG G1y	AAA Lys	GAT' Asp
GGG	CCC	TTC	CCG Pro	$_{\rm GGT}$	GAG Glu	TGC	AAT	CAG Gln	GCT Ala
GCC	CAC His	ATC Ile	CTT	GGA Gly	AAA Lys	CGG Arg	AAG Lys	ATA Ile	CTG Leu
AAA Lys	66C G1y	\mathtt{TAC}	CGC Arg	GAA Glu	TTG	CTT Leu	T.T.C Phe	AAG Lys	TCA
GCG Ala	TGG	AGG	$_{\rm GGC}$	CAA Gln	CGC Arg	GTG Val	TGG	ATC Ile	GCG Ala
GCG Ala	GCC Ala	AGC	CCC	CCT Pro	CCC Pro	CTA Leu	AAG Lys	AAC Asn	AAA Lys
TGG	GGC Gly	GAC	GGG Gly	GAA Glu	CCT Pro	AAA Lys	TTC Phe	GAA Glu	AGC
GTG Val	CTG	GAG Glu	66C 61y	CCG Pro	TTG Leu	TCC	AAG Lys	CCA Pro	ATT Ile
CAA	CGC	AAG Lys	AGC	666 61y	GCC Ala	$_{\rm GLY}^{\rm GGT}$	CTC	AAA Lys	CGC Arg
CAT His	GTG Val	CTC	AGC	GAC Asp	TGC	GCA Ala	TCT Ser	AAC Asn	CTT Leu
CCTGCAG	ACC Thr	CGC Arg	AAC	CGA Arg	CGG	GTG Val	TCC	AAG Lys	GAA Glu
CCT	CTC	GGG	GCC Ala	TCT Ser	CAA Gln	TCT Ser	TAC Tyr	CGA Arg	TCA

FIG. 28E

Nucleotide Sequences & Deduced Amino Acid Sequences of GGF2BPP3

YEAST CHICKEN RABBIT BOVINE DOG MOUSE RAT MONKEY HUMAN





474

522

FIG. 31A

Coding Segments of Glial Growth Factor/Heregulin Gene

420	AAACTTTTCC CGAAGCCGAT CCCAGCCCTC GGACCCAAAC TTGTCGCGCG TCGCCTTCGC AAACTTTTCC CAAACCGAT CCGAGCCTT GGACCAAAC TTGTCGCGCG TCGCCTTCGC TCGCCTTCGCCTT GGACCAAA
360	GCTCCCCCC ACGCCGCGCG CGCCTCGGCC CGGTCGCTGG CCCGCCTCCA CTCCGGGGAC
300	AGTCCCAGGT GGCCCGGACC GCACGTTGCG TCCCCGCGCT CCCCGCCGGC GACAGGAGAC
240	CCAGCGGCGC GCCAGCAGGA GCCACCCCGC GAGNCGTGCG ACCGGGACGG AGCGCCCGCC
180	TGCGAGCGCG CCGGACCGAG GCAGCGACAG GAGCGGACCG CGGCGGAAC CGAGGACTCC
120	GECGGCTGCC CAGGCGATGC GAGCGCGGGC CGGACGGTAA TCGCCTCTCC CTCCTCGGGC
09	AGTITCCCCC CCCAACTIGT CGGAACTCTG GGCTCGCGCG CAGGGCAGGA GCGGAGCGGC
	CODING SEGMENT F: (SEQ ID NO: 136 (bovine) and 173 (human))

Arg Aga 	AAA K		_		_	
Arg CGC		Ser	TCC	<u>=</u>	TCC	
Glu GAG	_	G1y	GGC	=	CGC	
Ser TCG	_	Arg	CGA	<u> </u>	CGA	
Met ATG	~	Asp	GAC		GAG	Ē
		Lys	AAG	<u> </u>	AAG	
TCGGGCGAG	TCCGGCGAG	Lys	AAG	=	AAG	
		G1y	ggC		AAG	×
ACTT(.CGT(G1y	ggC	<u> </u>	CGC	
CGTGCACTTC	3CTC.	Lys	AAG	<u> </u>	AAG	
		G1y	GGG	<u> </u>	GGG	
ccececagae	CCCCGTAGAG	Lys	AAG		AAA	
) 	SCGCC	G1y	CCC	=	CGC	
	•	Lys	AAA	<u> </u>	AGA	K
GGGAGCCGT	CGAGAGCCGT	Gly	ggC	=	GGC	
) 	CGA(Glu	GAA	=	GAA	

Ala	9		g
		=	
		=	
Pro	CCG		CAG
		_	
G1y	CCC	=	CCC
Ala	GCT		CCG
Ala	gCG	_	929
Pro	CCC	=	TCC
Pro	CCC	=	900
Lys	AAG	=	AAG
Lys	AAG		AAG

FIG. 31E

137)
NO:
ID
(SEQ
四
SEGMENT
CODING

4	9.6	143	191	239	252
TCG Ser	TCC Ser	CCC Pro	CCC Pro	GCT Ala	,*
GAC Asp	CCC Pro	GAG Glu	CTT Leu	GGT Gly	
AAG Lys	TTC Phe	ATG Met	CTC	CCG Pro	
$\begin{array}{c} \text{AAG} \\ \text{L}\gamma\text{s} \end{array}$	GCC Ala	TTC	AGC	CAG	
TTG	CCC Pro	TTC Phe	CCG Pro	${\tt GGT}$	
GGC Gly	CAC His	ATC Ile	CTT Leu	GGA Gly	
GGG	GGC Gly	TAC	CGC Arg	GAA Glu	
GCC Ala	TGG	AGG Arg	GGC Gly	CAA Gln	
AAA Lys	GCC	AGC Ser	CCC Pro	CCT	
GCG Ala	${\tt GGC}$	GAC Asp	$\frac{\text{GGG}}{\text{G1y}}$	GAA Glu	
GCG Ala	CTG Leu	GAG Glu	GGC Gly	CCG Pro	
TGG	CGC Arg	AAG Lys	AGC Ser	$\frac{\text{GGG}}{\text{Gly}}$	Ö
GTG Val	GTG Val	CTC	AGC Ser	GAC Asp	TGC Cys
CAN Gln	ACC Thr	CGC	AAC Asn	CGA Arg	CGG Arg
CAT His	CTC	$_{\rm GIY}^{\rm GGG}$	GCC	TCT Ser	CAA Gln
CC	CTG Leu	TGC	GAG Glu	CCC Pro	GTG

FIG. 31C

CODING SEGMENT B: (SEQ ID NO: 138 (bovine, top) and 174 (human, bottom)

Ala GCA ||| GCA Val GTG GCT Glu GAG || GAA Gln CAG ||| CAG Ser AGT Glu Met Lys 9
GAG ATG AAG 7
||| ||| || ||
GAG ATG AAA 7 Lys AAA ||| AAA Leu TTG Arg CGC || CGA Pro Pro CCT ||| CCT Leu TTG TTG 3 - 3

Ser TCT |--Ser TCC |--Tyr TAC ||| TAC Glu GAA ||| GAA Ser TCT TCT Ser AGT Thr ACC ||| Glu GAG || GAA Arg CGG CTT CTT CTT CTT Val GTG || GTC Leu CTA ||| Lys AAA AAA Ser TCC TCC Gly GGT ||| GGT

Lys Asn AAG AAC || || AAA AAC Arg CGA CGA Ser AGC | AAT Glu Leu GAA TTA ||| || GAA TTG Ser AGT - AAT N G17 GGG GGG GGG Asn AAT ||| Lys AAG AAG Phe TTC ||| Trp TGG ||| Lys AAG ||| AAG Phe TTC TTC Lys AAG | AGA R Leu CTC |---

G1y GG — Pro CCG Arg AGG | | AAG Lys AAA ||| AAA Gln CAG Ile ATA ||| Lys AAG ||| AAG Ile ATC ATC Asn AAC || AAT Gln CAA ||| CAA Pro CCA ||| CCA Lys AAA |||| AAA

32/6.

FIG. 31D

FIG. 31E

CODING SEGMENT A': (SEQ ID NO: 140)

TCTAAAACTA CAGAGACTGT ATTTTCATGA TCATCATAGT TCTGTGAAAT ATACTTAAAC	CTTAAAC 60
CGCTTTGGTC CTGATCTTGT AGG AAG TCA GAA CTT CGC ATT AGC AAA GCG Lys Ser Glu Leu Arg Ile Ser Lys Ala	GCG 110 Ala
CTG GCT GAT TCT GGA GAA TAT ATG TGC AAA GTG ATC AGC AAA CTA Leu Ala Asp Ser Gly Glu Tyr Met Cys Lys Val Ile Ser Lys Leu	A CTA 158 s Leu
GAC AGT GCC TCT GCC AAC ATC ACC ATT GTG GAG TCA AAC CASP Ser Ala Ser Ala Asn Ile Thr Ile Val Glu Ser Asn C	c GGT 206 n Gly
TGC CTA CTG CGT GCT ATT TCT CAG TCT CTA AGA GGA GTG Cys Leu Leu Arg Ala Ile Ser Gln Ser Leu Arg Gly Val	3 ATC 254 1 Ile
GTA TGT GGT CAC ACT TGAATCACGC AGGTGTGTGA AATCTCATTG Val Cys Gly His Thr	302
TGAACAAATA AAAATCATGA AAGGAAAACT CTATGTTTGA AATATCTTAT GGGTCCTCCT	PCCTCCT 362
GTAAAGCTCT TCACTCCATA AGGTGAAATA GACCTGAAAT ATATATAGAT TATTT	rT 417

47

95

FIG. 31F

(human))
176
and
(bovine)
141
NO:
ID
(SEQ
 U
3 SEGMENT G:
CODING

Ser	TCT	=	TCT
		=	\mathtt{GTG}
Tyr	TAT	=	\mathtt{TAT}
Ala	GCG		GCA
Thr			GGA G
		=	GAA
		=	ACT
Ser	TCA	=	TCA
		=	-
Pro	CCA	=	CCA
Met	ATG	=	ATG
Gly	GGC	=	GGT
Thr	ACT		ACT
Thr	ACC		ATC I
Ile	ATC	\equiv	ATC
Glu	AG	=	AG

Thr	ACT	=	ACT
Asn	AAT	=======================================	AAT
Thr	GAA GGA ACA	=	GGA GCA AAT
G1y	GGA	=	GGA
Thr Glu Gly		=	GAA
Thr	ACA	=	ACA
Ser	TCA		TCC
Val S	TCA GTA	=	GTA
Ser	TCA	=	TCA
Arg Ile Ser	ATA		ATA
Arg	AGA	=	AGA
Ile	TCT CCC ATT.	=	CCC ATT AGA
Pro	\mathcal{CCC}	=	$\mathcal{O}\mathcal{O}\mathcal{O}$
Ser Pro			TCT
Glu	GAG	= =	GAG
Ser	TCA		TCA
		٠.	

Ser Ser Ser
TCT TCA T
| | | | | | |
TCT TCA T

47

FIG. 31G

(human)
177
and
(bovine)
160
: ON
H
(SEQ ID
::
ODING SEGMENT
CODING

		•
Ala GCA	909	Val GTG GTG
Cys TGT	TGT	Met ATG
Lys AAG	AAA	Phe TTC TTC
Val GTC	GTA	Cys TGC TGC
CTT	CTT	Glu GAG GAG
His CAT	CAT	G1y GGC
Ser AGC	AGC	Gly GGA [[]
Thr ACA	ACA	Asn AAT
G1 <i>y</i> GGG		Val GTG GTG
Ala GCT	ACT T	Cys TGT TGT
Thr ACA	ACC	Phe TTC
Ser TCT	TCC	Thr ACT
Thr ACA	ACA	Lys AAA AAA
Ser TCC	TCT	Glu GAG
Thr ACA	ACA	Lys AAG AAG
) —	CŢ	Glu GAG GAG

95

Cys	TGC	=
Leu	TTG	_
m TYr	TAC	=
Arg	AGA	=
Ser	TCA	_
Pro	CCC	=
Asn	AAT	=
Ser	TCA	
Leu	CTT	=
Asp	GAC	=
Lys	AAA	=

AAA GAC CTT TCA AAC CCC TCG AGA TAC TTG TGC

FIG. 31H

CODING SEGMENT C/D: (SEQ ID NO: 142 (bovine) and 178 (human))

Pro Glu Asn Val 1 GAG AAT GTG (Cys (TGT) Arg AGA ||| Ala GCG Gly GGA Thr ACT ||| Phe TTC Gly GGA Pro CCT | | CCT Gln CAA Cys TGC Lys (
AAG |
AAG |
AAG

Met Lys Val Gln Thr Gln Glu ATG AAA GTC CAA ACC CAA GAA ||| ||| ||| || || || || || ||| ATG AAA GTC CAA AAC CAA GAA

115 211	CODING SEGMENT $\leq D'$ (SEQ ID NO: 143 (bovine) and 179 (human))	
<u>.</u>	Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met AAG TGC CCA AAT GAG TTT ACT GGT GAT CGC TGC CAA AAC TAC GTA ATG	48
	Ala Ser Phe Tyr GCC AGC TTC TAC GCC AGC TTC TAC	09
· •		
iG. 31J	CODING SEGMENT D: (SEQ ID NO: 144 (bovine) and 180 (human)) Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro Glu * AGT ACG TCC ACT CCC TTT CTG TCT CTG CCT GAA TAG	36
	Ace ice Aci cee iri cie ici cie cei GAA	
IG. 31K	CODING SEGMENT D': (SEQ ID NO: 145 (bovine)) Lys His Leu Gly Ile Glu Phe Met Glu	27
		i

	48	96	144	192	240	288
CODING SEGMENT H: (SEQ ID NO: 146 (bovine) and 181 (human))	FIG. 31L Lys Ala Glu Glu Leu Tyr Gln Lys Arg Val Leu Thr Ile Thr Gly Ile AAA GCG GAG GAG CTC TAC CAG AAG AGA GTG CTC ACC ATT ACC GGC ATT	Cys lle Ala Leu Leu Val Val Gly Ile Met Cys Val Val Val Tyr Cys TGC ATC GCG CTG CTC GTG GTT GGC ATC ATG TGT GTG GTG TAC TGC 	Lys Thr Lys Lys Gln Arg Lys Lys Leu His Asp Arg Leu Arg Gln Ser Aaa Acc Aag Aaa Caa CGG Aaa Aag CTT CAT GAC CGG CTT CGG CAG AGC 11	Arg Ser Glu Arg Asn Thr Met Met Asn Val Ala Asn Gly Pro His CGG TCT GAA AGA AAC ACC ATG ATG AAC GTA GCC AAC GGG CCC CAC 	His Pro Asn Pro Pro Glu Asn Val Gln Leu Val Asn Gln Tyr Val CAC CCC AAT CCG CCC CCC GAG AAC GTG CAG CTG GTG AAT CAA TAC GTA	Ser Lys Asn Val Ile Ser Ser Glu His Ile Val Glu Arg Glu Ala Glu TCT AAA AAT GTC ATC TCT AGC GAG CAT ATT GTT GAG AGA GAG GCG GAG
Ī	L L					

FIG. 31M

94

141

46

FIG. 31N

CODING SEGMENT K: (SEQ ID NO: 161)

TCC	TCC	AG
AGA Arg	TCT Ser	GGA Glv
CAC His	GCT Ala	TTA
GCC Ala	AGA Arg	CCT
AAG Lys	CTT Leu	TGG
AAC Asn	CAT His	CCT
AGA Arg	ACT Thr	ACC Thr
AGG Arg	GCA Ala	AAG Lys
CTA Leu	TCC	TCT Ser
GAG Glu	CTT Leu	TTC
GCT Ala	CAG Gln	TCA Ser
ATA Ile	ATC Ile	GCT Ala
CTT Leu	CAG Gln	$\frac{\text{TGG}}{\text{Trp}}$
AAC Asn	ATG Met	CAT His
CAT His	TGC Cys	CCC Pro
Ø	AAA Lys	ATT Ile

		CODING		SEGMENT	AT L	L: (SEQ	EQ ID	ON C	NO: 147	7
		TYY	Val	Ser	Ala	Met	Ala Met Thr Thr	Thr	Pro A	Ø
	G	\mathtt{TAT}	GTA	TCA	TCA GCA ATG	ATG	ACC	ACC	CCG	G
ر ا ا	_	=	_	<u> </u>	=		=	<u>=</u>	=	_

(bovine) and 182 (human))

Asp GAT GAT	Pro CCG [CCA
_	Ser TCC TCT
CTA	Met ATG
Pro CCT 	
Ser TCA TCA	Glu GAA
Met S ATG 1 ATG 1	Ser TCG TCG
	Pro CCT
CGT CGT	Pro CCC
Ala GCT GCT	_
Pro CCG 	S Ser
Thr ACC (Lys AAG AAA
	Pro CCC
Thr ACC	Ser TCC
Met ATG 	Ser S AGC T
Ala GCA 	
Ser TCA (Pro CCA CCA
-	Thr ACG
r Val F GTA	His CAC
TY <i>r</i> TAT TAT	Phe H TTC C
<u>ი</u> — ი	17 — FT

94

Pro	CCC	=	$\mathcal{C}\mathcal{C}\mathcal{C}$	Leu	CTG	=	CTG
Ser	AGT		AGC	Arg	CGG		AGG
Val	GTC	<u>=</u>	GTC	Pro	CCA	_	CCA
		<u>=</u>	_	Pro	CCA	=	CCA
Met	ATG	=	ATG	Thr	ACG	=	ACA
Ser	TCC		TCC	Val	GTG	<u> </u>	GTG
		=		Leu	CTT		CTC
Met	ATG		ATG	Leu	CIC		CTT
				Leu	CTG	=	CTA
Val	GTC	-	GTG	Pro	CCC		CCT
Thr	ACG	$\stackrel{\cdot}{=}$	ACG	Arg	AGA	=	AGA
Thr	ACG	_	ATG M	Glu	GAG	\equiv	GAG
Ser	AGC	=	AGC	Glu	GAG		GAA
		=		Glu	GAA	_	GAA
Val	GTG	=	GTG	Val	GTG	=	ATG
Pro	CCC	=	CCC	Phe	TTC	=	TTC

Phe His TTC CAC TTC CAC TTC CAC TTC AGG TTG AGG	
Phe TTC	
Ser TCG TCC Pro CCC	
Asn AAC AGC Ser AGC AGC AGC	
Phe TTC	'
Gln CAA	
Gln CAG CAG CAG CAG CAG CAG CTG CTG CTC	
Ala GCC CCT P Ser AGC AGC	
His CAC CAC ASD ASD AAC AAC	
His CAC	
Asp GAC GAC GAG GAG CAG	ì
TYr TAT TTT F His CAT	
AAG K Ala GCG GCG GCG	
Lys AAG AAG CCC	
Glu GAG GAG ASD AAC	
Arg CGG CGG CYS TGC	-

382

478

334

FIG. 31P

Ala GCT 	Arg AGA AGA	Asn AAC AAC	Arg AGA AGA
Pro CCA []] CCA	Lys AAA AAA	Asn AAC AGC S	Glu GAA GAA
Glu GAA GAG	Ala GCC GCC	Asp GAC GAC	Asp GAT GAT
Tyr TAC TAC	Arg CGG CGG	Met ATG GTG	Glu GAG GAA
Glu GAG GAG	Arg CGG CGG	Glu GAA GAA	Thr ACA ACA
Gln CAG [.] CAA	Ser AGC 	Leu TTG TTG	Glu GAA GAA
Thr ACC [11] ACC	Ser AGC	Arg AGG AGA	Ser AGC
Thr ACG 	Asn AAC 	His CAC 	Glu GAG GAG
Glu GAA GAA	Thr ACC II GCC A	Ala GCC GCT	Ser TCA TCA
Tyr TAT TAT	Leu CTC 	Ile ATT ATT	Asn AAC
Glu GAA GAG	Lys AAA AAA	His CAC CAC	Ser AGT AGT
Glu GAG GAG	Lys AAG AAG	Gly GGT GGC	Ser AGC AGC
Asp GAT GAT	Val GTT GTT	Asn AAT AAT	Asp GAC CAG
Glu GAG GAG	Pro CCG 	Pro	Ala GCT TCC S
Val GTG 	Glu GAG GAG	Lys AAG AAG	G1y GGC H
Ile ATA 	Gln CAA CAA	Thr ACC 	Thr ACA [1] ACA

526	574	622	672	718	733
Val Gly Glu Asp Thr Pro Phe Leu Ala Ile Gln Asn Pro Leu GTA GGA GAA GAT ACG CCT TTC CTG GCC ATA CAG AAC CCC CTG	Leu Glu Ala Ala Pro Ala Phe Arg Leu Val Asp Ser CTC GAG GCC CCT GCC TTC CGC CTG GTC GAC AGC 	Thr Gly Gly Phe Ser Pro Gln Glu Glu Leu Gln Ala Arg Leu AcA GGC GGC TTC TCT CCG CAG GAA GAA TTG CAG GCC AGG CTC	Gly Val Ile Ala Asn Gln Asp Pro Ile Ala Val * GGT GTA ATC GCT AAC CAA GAC CCT ATC GCT GTC TAA AAC CGA AAT ACA [ATA GAT TCA CCT GTA AAA CTT TAT TTT ATA TAA TAA AGT ATT	AA ATT
O					

FIG. 32A GGF2BPP5 Nucleotide Sequence & Deduced Protein Sequence

SEQ ID NO: 148:

09	120	180	240	300	360	420	475	523	571	619	667	715	763	811
AGTTTCCCCC CCCAACTTGT CGGAACTCTG GGCTCGCGCG CAGGGCAGGA GCGGAGCGGC	GGCGGCTGCC CAGGCGATGC GAGCGCGGGC CGGACGGTAA TCGCCTCTCC CTCCTCGGGC	TGCGAGCGCG CCGGACCGAG GCAGCGACAG GAGCGGACCG CGGCGGGAAC CGAGGACTCC	CCAGCGGCGC GCCAGCAGGA GCCACCCCGC GAGCGTGCGA CCGGGACGGA GCGCCCGCCA	GTCCCAGGTG GCCCGGACCG CACGTTGCGT CCCCGCGCTC CCCGCCGGCG ACAGGAGACG	CTCCCCCCCA CGCCGCGC GCCTCGGCCC GGTCGCTGGC CCGCCTCCAC TCCGGGGACA	AACTTTTCCC GAAGCCGATC CCAGCCCTCG GACCCAAACT TGTCGCGCGT CGCCTTCGCC	GGGAGCCGTC CGCGCAGAGC GTGCACTTCT CGGGCGAG ATG TCG GAG CGC AGA	GAA GGC AAA GGC AAG GGG AAG GGC GGC AAG AAG	AAG CCC GTG CCC GCG GCT GGC GGC CCG AGC CCA GCC TTG CCT	LYS LYS FIO VAL FIO ALA ALA GIY GIY FIO SET FIO ALA LEU FIO FIO CGC TTG AAA GAG ATG AAG ATG CAG GAG TCT GTG GCA GGT TCC AAA CTA Arg Leu Lys Glu Met Lys Ser Gln Glu Ser Val Ala Gly Ser Lys Leu	GTG CTT CGG TGC GAG ACC AGT TCT GAA TAC TCC TCT CTC AAG TTC AAG Val Leu Arg Cys Glu Thr Ser Ser Glu Tyr Ser Ser Leu Lys Phe Lys	TGG TTC AAG AAT GGG AGT GAA TTA AGC CGA AAG AAC AAA CCA CAA AAC Trp Phe Lys Asn Gly Ser Glu Leu Ser Arg Lys Asn Lys Pro Gln Asn	ATC AAG ATA CAG AAA AGG CCG GGG AAG TCA GAA CTT CGC ATT AGC AAA Ile Lys Ile Gln Lys Arg Pro Gly Lys Ser Glu Leu Arg Ile Ser Lys	GCG TCA CTG GCT GAT TCT GGA GAA TAT ATG TGC AAA GTG ATC AGC AAA Ala Ser Leu Ala Asp Ser Gly Glu Tyr Met Cys Lys Val Ile Ser Lys

FIG. 32B

GGF2BPP5 Nucleotide Sequence & Deduced Protein Sequence

859	907	955	1003	1051	1099	1147	1193	1253	1313	1373	1433	1493	1553	1613	1654
CTA GGA AAT GAC AGT GCC TCT GCC AAC ATC ACC ATT GTG GAG TCA AAC Leu Gly Asn Asp Ser Ala Ser Ala Asn Ile Thr Ile Val Glu Ser Asn	GAG ATC ACC ACT GGC ATG CCA GCC TCA ACT GAG ACA GCG TAT GTG TCT Glu Ile Thr Thr Gly Met Pro Ala Ser Thr Glu Thr Ala Tyr Val Ser	TCA GAG TCT CCC ATT AGA ATA TCA GTA'TCA ACA GAA GGA ACA AAT ACT Ser Glu Ser Pro Ile Arg Ile Ser Val Ser Thr Glu Gly Thr Asn Thr	TCT TCA TCC ACA TCC ACA TCT ACA GCT GGG ACA AGC CAT CTT GTC AAG Ser Ser Ser Thr Ser Thr Ser Thr Ala Gly Thr Ser His Leu Val Lys	TGT GCA GAG AAG GAG AAA ACT TTC TGT GTG AAT GGA GGC GAG TGC TTC Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn Gly Gly Glu Cys Phe	ATG GTG AAA GAC CTT TCA AAT CCC TCA AGA TAC TTG TGC AAG TGC CCA Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr Leu Cys Lys Cys Pro	AAT GAG TTT ACT GGT GAT CGC TGC CAA AAC TAC GTA ATG GCC AGC TTC Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala Ser Phe	TAC AGT ACG TCC ACT CCC TTT CTG TCT CTG CCT GAA TAGGCGCATG Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro Glu	CTCAGTCGGT GCCGCTTTCT TGTTGCCGCA TCTCCCCTCA GATTCAACCT AGAGCTAGAT	GCGTTTTACC AGGTCTAACA TTGACTGCCT CTGCCTGTCG CATGAGAACA TTAACACAAG	CGATTGTATG ACTTCCTCTG TCCGTGACTA GTGGGCTCTG AGCTACTCGT AGGTGCGTAA	GGCTCCAGTG TTTCTGAAAT TGATCTTGAA TTACTGTGAT ACGACATGAT AGTCCCTCTC	ACCCAGTGCA ATGACAATAA AGGCCTTGAA AAGTCTCACT TTTATTGAGA AAATAAAAT	CGTTCCACGG GACAGTCCCT CTTCTTTATA AAATGACCCT ATCCTTGAAA AGGAGGTGTG	TTAAGTIGTA ACCAGTACAC ACTIGAAATG ATGGTAAGTT CGCTTCGGTT CAGAATGTGT	TCTTTCTGAC AAAAAAAAAAAA AAAAAAAA A

FIG. 33A

GGF2BPP2 Nucleotide Sequence & Deduced Protein Sequence

SEQ ID NO: 149:

48	96	144	192	240	288	336	384	432	480	528
GGG GGC TTG AAG AAG GAC TCG CTG	GGC CAC CCC GCC TTC CCC TCC TGC	TAC ATC TTC TTC ATG GAG CCC GAG	CGC CTT CCG AGC CTC CTT CCC CCC	GAA GGA GGT CAG CCG GGT GCT GTG	AAA GAG ATG AAG AGT CAG GAG	CGG TGC GAG ACC AGT TCT GAA	AAG AAT GGG AGT GAA TTA AGC	ATA CAG AAA AGG CCG GGG AAG	CTG GCT GAT TCT GGA GAA TAT	AAT GAC AGT GCC TCT GCC AAC
jly Gly Leu Lys Lys Asp Ser Leu	Gly His Pro Ala Phe Pro Ser Cys	Tyr Ile Phe Phe Met Glu Pro Glu	Arg Leu Pro Ser Leu Leu Pro Pro	Glu Gly Gly Gln Pro Gly Ala Val	Lys Glu Met Lys Ser Gln Glu	Arg Cys Glu Thr Ser Ser Glu	Lys Asn Gly Ser Glu Leu Ser	Ile Gln Lys Arg Pro Gly Lys	Leu Ala Asp Ser Gly Glu Tyr	Asn Asp Ser Ala Ser Ala Asn
AAA GCC GC	GCC TGG G(AGC AGG TA	CCC GGC CC	CCT CAA GA	CCC CGC TTG	CTA GTG CTT	AAG TGG TTC	AAC ATC AAG	AAA GCG TCA	AAA CTA GGA
Lys Ala G	Ala Trp G	Ser Arg TA	Pro Gly A1	Pro Gln Gl	Pro Arg Leu	Leu Val Leu	Lys Trp Phe	Asn Ile Lys	Lys Ala Ser	Lys Leu Gly
GCG GCG	CTG GGC	GAG GAC	GGC GGG	CCG GAA	TTG CCT	TCC AAA C	AAG TTC A	CCA GAA A	ATT AGC AZILLE Ser LY	ATC AGC AA
Ala Ala	Leu Gly	Glu Asp	Gly Gly	Pro Glu	Leu Pro	Ser Lys L	Lys Phe L	Pro Glu A		Ile Ser Ly
CAN GTG TGG	ACC GTG CGC	CGC CTC AAG	AAC AGC AGC	CGA GAC GGG	CGG TGC GCC	GTG GCA GGT	TCC TCT CTC	AAG AAC AAA	GAA CTT CGC	TGC AAA GTG
Gln Val Trp	Thr Val Arg	Arg Leu Lys	Asn Ser Ser	Arg Asp Gly	Arg Cys Ala	Val Ala Gly	Ser Ser Leu	Lys Asn Lys	Glu Leu Arg	Cys Lys Val
CAT (His (CTC A	GGG C	GCC A	TCT C	CAA C Gln A	TCT G	TAC T	CGA A Arg L	TCA G	ATG TO Met Cy

FIG. 33B

GGF2BPP2 Nucleotide Sequence & Deduced Protein Sequence	
ATC ACC ATT GTG GAG TCA AAC GCC ACA TCC ACA TCT ACA GCT GGG ACA 5 Ile Thr Ile Val Glu Ser Asn Ala Thr Ser Thr Ser Thr Ala Gly Thr	576
AGC CAT CTT GTC AAG TGT GCA GAG AAG GAG AAA ACT TTC TGT GTG AAT Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn	624
GGA GGC GAG TGC TTC ATG GTG AAA GAC CTT TCA AAT CCC TCA AGA TAC Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr	672
TTG TGC AAG TGC CAA CCT GGA TTC ACT GGA GCG AGA TGT ACT GAG AAT Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn	720
GTG CCC ATG AAA GTC CAA ACC CAA GAA AAG TGC CCA AAT GAG TTT ACT Val Pro Met Lys Val Gln Thr Gln Glu Lys Cys Pro Asn Glu Phe Thr	768
GGT GAT CGC TGC CAA AAC TAC GTA ATG GCC AGC TTC TAC AGT ACG TCC 81 Gly Asp Arg Cys Gln Asn Tyr Val Met Ala Ser Phe Tyr Ser Thr Ser	816
ACT CCC TTT CTG TCT CTG CCT GAA TAGCGCATCT CAGTCGGTGC CGCTTTCTTG 87 Thr Pro Phe Leu Ser Leu Pro Glu	870
ITGCCGCATC TCCCCTCAGA TTCCNCCTAG AGCTAGATGC GTTTTACCAG GTCTAACATT 93	930
SACTGCCTCT GCCTGTCGCA TGAGAACATT AACACAAGCG ATTGTATGAC TTCCTCTGTC 99	066
CGTGACTAGT GGGCTCTGAG CTACTCGTAG GTGCGTAAGG CTCCAGTGTT TCTGAAATTG 105	1050
ATCTTGAATT ACTGTGATAC GACATGATAG TCCCTCTCAC CCAGTGCAAT GACAATAAAG 111	1110
3CCTTGAAAA GTCAAAAAAA AAAAAAAAA	1140

FIG. 34A

GGF2BPP4 Nucleotide Sequence & Deduced Protein Sequence

SEQ ID NO: 150:

G AAG TCA GAA CTT CGC ATT AGC AAA GCG TCA CTG GCT GAT TCT GGA GAA Lys Ser Glu Leu Arg Ile Ser Lys Ala Ser Leu Ala Asp Ser Gly Glu TYR ATG TGC AAA GTG ATC AGC AAA CTA GGA AAT GAC AGT GCC TCT GCC TYR Met Cys Lys Val Ile Ser Lys Leu Gly Asn Asp Ser Ala Ser Ala AAC ATG TGC ATT GTG GAG TCA AAC GCC ACA TCC ACA TCT ACA GCT GCG Asn Ile Thr Ile Val Glu Ser Asn Ala Thr Ser Thr Ala Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Thr Phe Cys Val AAT GGA GGC CAT CTT GTG AAG TGT AAA GCC TT TCA AAT TCC TGT GTG Asn Gly Gly Asp Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg TYC TTG TGC AAG TGC CAA CTC GAA TTC GLY ATG CTC TAC ASN Gly Gly Asp Cys CAA ACT CAA AAA GCC GAG GGG GGG CTC TAC ASN Val Bro Met Lys Val Gln Thr Glu Lys Ala Glu Glu Leu Tyr CAG AAG AGG CTC ATG TGT GAT GTG TAC AAT TGC AAT AAG GCG AAA GTG CCA ATG TGC CAA ACC CAA AAA GCG GAG GTG TTC TAC ASN Val Bro Met Lys Val Gln Thr Glu Lys Ala Glu Glu Leu Val GLI Lys Arg Val Leu Thr Ile Thr Gly Ile Cys Ile Ala Leu Leu Val GTT GGC ATG TGT GTG GTG GTG TAC TGC AAA ACC AAA AAC AAA AAG CTT CAT GTG GTG GTG TAC TGC AAA ACC AAA AAC AAA AAG ATG TGT GTG GTG GTG TAC TGC AAA ACC AAA AAA CTG AAA AAG ATG TGT GTG GTG GTG TAC TGC AAA AAC AAA AAG AAG ATG TGT GTG GTG GTG TAC TGC AAA AAC AAA AAG AAG AAG AAG AAG AAG AAG AAG AAG	49	26	145	193	241	289	337	385	433	481	529	577
OO HA HA CO OO AA HOO	AAG TCA GAA CTT CGC ATT AGC AAA GCG TCA CTG GCT GAT TCT GGA	ATG TGC AAA GTG ATC AGC AAA CTA GGA AAT GAC AGT GCC TCT GC	ATC ACC ATT GTG GAG TCA AAC GCC ACA TCC ACA TCT ACA GCT GGG	AGC CAT CTT GTC AAG TGT GCA GAG AAG GAG AAA ACT TTC TGT GTG	GGA GGC GAC TGC TTC ATG GTG AAA GAC CTT TCA AAT CCC TCA AGA	TTG TGC AAG TGC CAA CCT GGA TTC ACT GGA GCG AGA TGT ACT GAG	GTG CCC ATG AAA GTC CAA ACC CAA GAA AAA GCG GAG GAG CTC TAC	AAG AGA GTG CTC ACC ATT ACC GGC ATT TGC ATC GCG CTG CTC GTG	GGC ATC ATG TGT GTG GTC TAC TGC AAA ACC AAG AAA CAA CGG	AAG CTT CAT GAC CGG CTT CGG CAG AGC CTT CGG TCT GAA AGA AAC	ATG ATG AAC GTA GCC AAC GGG CCC CAC CAC CCC AAT CCG CCC CCC	AAC GTG CAG CTG GTG AAT CAA TAC GTA TCT AAA AAT GTC ATC TCT
	Lys Ser Glu Leu Arg Ile Ser Lys Ala Ser Leu Ala Asp Ser Gly	Met Cys Lys Val Ile Ser Lys Leu Gly Asn Asp Ser Ala Ser Al	Ile Thr Ile Val Glu Ser Asn Ala Thr Ser Thr Ser Thr Ala Gly	Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val	Gly Gly Asp Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg	Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu	Val Pro Met Lys Val Gln Thr Gln Glu Lys Ala Glu Glu Leu Tyr	Lys Arg Val Leu Thr Ile Thr Gly Ile Cys Ile Ala Leu Leu Val	Gly Ile Met Cys Val Val Val Tyr Cys Lys Thr Lys Lys Gln Arg	Lys Leu His Asp Arg Leu Arg Gln Ser Leu Arg Ser Glu Arg Asn	Met Met Asn Val Ala Asn Gly Pro His His Pro Asn Pro Pro Pro	Asn Val Gln Leu Val Asn Gln Tyr Val Ser Lys Asn Val Ile Ser

FIG. 34B

GGF2BPP4 Nucleotide Sequence & Deduced Protein Sequence

625	673	721	769	817	865	913	961	1009	1057	1105	1153
AGT	CCC	AGC	AGC	CGT Arg	TAC	AGG Arg	GCA	AAG Lys	GCT Ala	CCC	CCC
ACC Thr	ACT Thr	GAA Glu	AGC Ser	CCT	TCC Ser	CTA	TCC Ser	TCT Ser	CCG	TCA Ser	ATG Met
TCC	CAG Gln	TCG	CAC His	GGC	GAC Asp	GAG Glu	CTT Leu	TTC Phe	ACC Thr	AAG Lys	TCC
TTT Phe	ACT Thr	ATT Ile	AGG Arg	GGA Gly	CCT	GCT Ala	CAG Gln	TCA	ACC Thr	CCC Pro	GTC
TCT Ser	GTC Val	ATC Ile	AGT Ser	TTG	ACC Thr	ATA Ile	ATC Ile	GCT Ala	ATG Met	TCC	ACG
AGC Ser	$_{ m Thr}$	AGC Ser	AAC Asn	$_{\rm GGC}$	GAA Glu	CTT Leu	CAG Gln	TGG	GCA	AGC Ser	ACG Thr
GAG Glu	ACT Thr	GAA Glu	GAA Glu	AAT Asn	AGA Arg	AAC Asn	ATG Met	CAT His	TCA	CCA	AGC
GCG Ala	TCC	ACT Thr	GTA Val	CTC Leu	GCC Ala	CAT His	TGC Cys	CCC Pro	GTA Val	ACG Thr	TCC
GAG	CAT His	CAC His	TCC Ser	CGT	CAT	AGA Arg	AAA Lys	ATT Ile	TAT	CAC	GTG Val
AGA Arg	CAT His	${\tt GGA} {\tt G1y}$	TCA	$_{\rm GGA}$	AGG Arg	GAA Glu	TCC Ser	TCC	AGG Arg	TTC	CCC Pro
GAG Glu	GCT Ala	AAT Asn	ATG Met	AGA Arg	CTC	AGT Ser	AGA Arg	TCT	GGA Gly	GAT	CCG Pro
GTT Val	ACA Thr	AGC Ser	GTG Val	CCG Pro	TTC Phe	CAT His	CAC Hìs	GCT Ala	TTA	GTA Val	TCC
ATT Ile	TCG Ser	TGG Trp	ATC Ile	GGC	AGC Ser	CCT. Pro	GCC Ala	AGA Arg	CCT Pro	CCT	ATG Met
CAT His	ACT Thr	AGC Ser	GTC Val	GGG	AAC Asn	TCT	AAG Lys	CTT Leu	TGG Trp	TCA	GAA Glu
GAG Glu	\mathtt{TAC}	CAC His	TCT Ser	ACT	TGT Cys	GAC Asp	AAC Asn	CAT	CCT Pro	ATG Met	TCG
AGC Ser	CAC His	AGT Ser	CAC His	CCG	GAA Glu	CGA Arg	AGA Arg	ACT Thr	ACC	CGT	CCT

FIG. 34C GGF2BPP4 Nucleotide Sequence & Deduced Protein Sequence

1393 1441 1537 1533 1633 1741	GAG TAC GAA CCA GCT CAA GAG CCG GTT AAG AAA CTC ACC AAC AGC AGC GLU Tyr Glu Pro Ala Glu Pro Val Lys Lys Leu Thr Asn Ser Ser CGG CGG CCAAA AGA ACA AG CCC AAT GGT CAC ATT GCC CAC AGG TTG ARG ATG ALG AS ASN Thr Lys Pro Asn Gly His Ile Ala His Arg Leu GAA ATG GAC AAC ACA GGC GCT GAC AGC AGT AAC TCA GAG AGC GAA GLU Met Asp Asn Asn Thr Gly Ala Asp Ser Ser Asn Ser Glu Ser Glu ACA GAG GAA GGA GAT ACG CCT TTC CTG GCC ATA CAC GTD AAC GAG GAG GAT GAG GAA GAG GAG GAG GAC GCC CTG GCC TTC CGC GCC GCC GCC GCC GC
4 4	AAA AGA ACC AAG CCC AAT GGT CAC ATT GCC CAC AGG Lys Arg Thr Lys Pro Asn Gly His Ile Ala His Arg AAC AAC ACA GGC GCT GAC AGC AGT AAC TCA GAG AGC ASn Asn Thr Gly Ala Asp Ser Ser Asn Ser Glu Ser
39	CCA GCT CAA GAG CCG GTT AAG AAA CTC ACC AAC AGC Pro Ala Glu Pro Val Lys Lys Leu Thr Asn Ser
1345	CCC TTG AGG ATA GTG GAG GAT GAG GAA TAT GAA ACG ACC CAG Pro Leu Arg Ile Val Glu Asp Glu Glu Tyr Glu Thr Thr Gln
1297	TCG TTC CAC TGC AAC CCC GCG CAT GAG AGC AAC AGC CTG CCC Ser Phe His Cys Asn Pro Ala His Glu Ser Asn Ser Leu Pro
1249	CCA CCA CGG CTG CGG GAG AAG TAT GAC CAC CAC GCC CAG CAA Pro Pro Arg Leu Arg Glu Lys Tyr Asp His His Ala Gln Gln
1201	GCG GTC AGT CCC TTC GTG GAA GAG GAG AGA CCC CTG CTC CTT Ala Val Ser Pro Phe Val Glu Glu Glu Arg Pro Leu Leu Leu

FIG. 35

GGF2bpp5 (SEQ ID NO: 151) KCAEKEKTFCVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCQNYVMASFY GGF2bpp4 (SEQ ID NO: 152) KCAEKEKTFCVNGGDCFMVKDLSNPSRYLCKCQPGFTGARCTENVPMKVQ (SEQ ID NO: 153) ECLRKYKDFCIH-GECKYVKELRAPS---CKCQQEYFGERCGEKSNKTHS hEGF

FIG. 36
200 kDa Tyrosine Phosphorylation
Compared with Mitogenic Activity

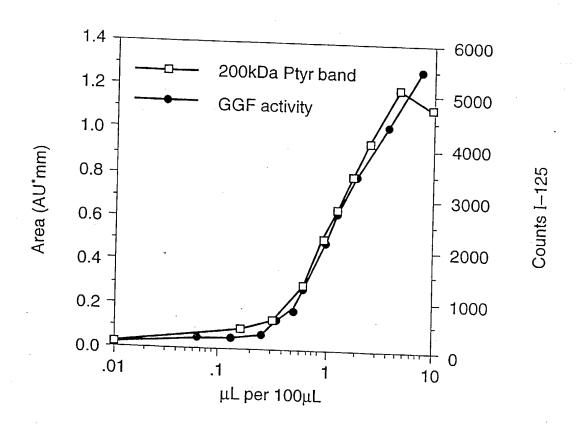


FIG. 37A GGF/Heregulin Splicing Variants

F-B-A'	F-E-B-A'
F-B-A-C-C/D-D	F-E-B-A-C-C/D-D
F-B-A-C-C/D-H	F-E-B-A-C-C/D-H
F-B-A-C-C/D-H-L	F-E-B-A-C-C/D-H-L
F-B-A-C-C/D-H-K-L	F-E-B-A-C-C/D-H-K-L
F-B-A-C-C/D-D'-H	F-E-B-A-C-C/D-D'-H
F-B-A-C-C/D-D'-H-L	F-E-B-A-C-C/D-D'-H-L
F-B-A-C-C/D-D'-H-K-L	F-E-B-A-C-C/D-D'-H-K-L
F-B-A-C-C/D'-D	F-E-B-A-C-C/D'-D
F-B-A-C-C/D'-H	F-E-B-A-C-C/D'-H
F-B-A-C-C/D'-H-L	F-E-B-A-C-C/D'-H-L
F-B-A-C-C/D'-H-K-L	F-E-B-A-C-C/D'-H-K-L
F-B-A-C-C/D'-D'-H	F-E-B-A-C-C/D'-D'-H
F-B-A-C-C/D'-D'-H-L	F-E-B-A-C-C/D'-D'-H-L
F-B-A-C-C/D'-D'-H-K-L	F-E-B-A-C-C/D'-D'-H-K-L
F-B-A-C-C/D-C/D'-D	F-E-B-A-C-C/D-C/D'-D
F-B-A-C-C/D-C/D'-H	F-E-B-A-C-C/D-C/D'-H
F-B-A-C-C/D-C/D'-H-L	F-E-B-A-C-C/D-C/D'-H-L
F-B-A-C-C/D-C/D'-H-K-L	F-E-B-A-C-C/D-C/D'-H-K-L
F-B-A-C-C/D-C/D'-D'-H	F-E-B-A-C-C/D-C/D'-D'-H
F-B-A-C-C/D-C/D'-D'-H-L	F-E-B-A-C-C/D-C/D'-D'-H-L
F-B-A-C-C/D-C/D'-D'-H-K-L	F-E-B-A-C-C/D-C/D'-D'-H-K-L
E.B.A.C.C.C.D.D	
F-B-A-G-C-C/D-D F-B-A-G-C-C/D-H	F-E-B-A-G-C-C/D-D
F-B-A-G-C-C/D-H-L	F-E-B-A-G-C-C/D-H
F-B-A-G-C-C/D-H-K-L	F-E-B-A-G-C-C/D-H-L
F-B-A-G-C-C/D-D'-H	F-E-B-A-G-C-C/D-H-K-L
F-B-A-G-C-C/D-D'-H-L	F-E-B-A-G-C-C/D-D'-H
F-B-A-G-C-C/D-D'-H-K-L	F-E-B-A-G-C-C/D-D'-H-L
F-B-A-G-C-C/D'-D	F-E-B-A-G-C-C/D-D'-H-K-L
F-B-A-G-C-C/D'-H	F-E-B-A-G-C-C/D'-D
F-B-A-G-C-C/D'-H-L	F-E-B-A-G-C-C/D'-H
F-B-A-G-C-C/D'-H-K-L	F-E-B-A-G-C-C/D'-H-L
F-B-A-G-C-C/D'-D'-H	F-E-B-A-G-C-C/D'-H-K-L F-E-B-A-G-C-C/D'-D'-H
F-B-A-G-C-C/D'-D'-H-L	F-E-B-A-G-C-C/D'-D'-H-L
F-B-A-G-C-C/D'-D'-H-K-L	F-E-B-A-G-C-C/D'-D'-H-K-L
F-B-A-G-C-C/D-C/D'-D	F-E-B-A-G-C-C/D-C/D'-D
F-B-A-G-C-C/D-C/D'-H	F-E-B-A-G-C-C/D-C/D'-H
F-B-A-G-C-C/D-C/D'-H-L	F-E-B-A-G-C-C/D-C/D'-H-L
F-B-A-G-C-C/D-C/D'-H-K-L	F-E-B-A-G-C-C/D-C/D'-H-K-L
F-B-A-G-C-C/D-C/D'-D'-H	F-E-B-A-G-C-C/D-C/D'-D'-H
F-B-A-G-C-C/D-C/D'-D'-H-L	F-E-B-A-G-C-C/D-C/D'-D'-H-L
F-B-A-G-C-C/D-C/D'-D'-H-K-L	F-E-B-A-G-C-C/D-C/D'-D'-H-K-
	0 C C/D C/D -D -H-K-

E-B-A-C-C/D-D

E-B-A-C-C/D-H

FIG. 37B

GGF/Heregulin Splicing Variants

E-B-A'

```
E-B-A-C-C/D-H-L
E-B-A-C-C/D-H-K-L
E-B-A-C-C/D-D'-H
E-B-A-C-C/D-D'-H-L
E-B-A-C-C/D-D'-H-K-L
E-B-A-C-C/D'-D
E-B-A-C-C/D'-H
E-B-A-C-C/D'-H-L
E-B-A-C-C/D'-H-K-L
E-B-A-C-C/D'-D'-H
E-B-A-C-C/D'-D'-H-L
E-B-A-C-C/D'-D'-H-K-L
E-B-A-C-C/D-C/D'-D
E-B-A-C-C/D-C/D'-H
E-B-A-C-C/D-C/D'-H-L
E-B-A-C-C/D-C/D'-H-K-L
E-B-A-C-C/D-C/D'-D'-H
E-B-A-C-C/D-C/D'-D'-H-L
E-B-A-C-C/D-C/D'-D'-H-K-L
E-B-A-G-C-C/D-D
E-B-A-G-C-C/D-H
E-B-A-G-C-C/D-H-L
E-B-A-G-C-C/D-H-K-L
E-B-A-G-C-C/D-D'-H
E-B-A-G-C-C/D-D'-H-L
E-B-A-G-C-C/D-D'-H-K-L
E-B-A-G-C-C/D'-D
E-B-A-G-C-C/D'-H
E-B-A-G-C-C/D'-H-L
E-B-A-G-C-C/D'-H-K-L
E-B-A-G-C-C/D'-D'-H
E-B-A-G-C-C/D'-D'-H-L
E-B-A-G-C-C/D'-D'-H-K-L
E-B-A-G-C-C/D-C/D'-D
E-B-A-G-C-C/D-C/D'-H
E-B-A-G-C-C/D-C/D'-H-L
E-B-A-G-C-C/D-C/D'-H-K-L
E-B-A-G-C-C/D-C/D'-D'-H
```

E-B-A-G-C-C/D-C/D'-D'-H-L E-B-A-G-C-C/D-C/D'-D'-H-L

FIG. 38 EGFL1

SEQ ID NO: 154:

Val Asn	AGA TAC 96 Arg Tyr	AAC TAC 144 Asn Tyr	CTG CCT 192 Leu Pro	198
Cys	TCA	CAA Gln	TCT Ser	
Phe	CCC Pro	TGC Cys	CTG Leu	
ACT	AAT Asn	CGC Arg	TTT Phe	
AAA Lys	TCA	GAT Asp	CCC Pro	
GAG Glu	CTT Leu	GGT	ACT Thr	
AAG Lys	GAC	ACT Thr	TCC Ser	
Glu	AAA Lys	TTT Phe	ACG Thr	
GCA	GTG Val	GAG Glu	AGT	
Cys	ATG Met	AAT Asn	TAC	
AAG Lys	TTC Phe	CCA Pro	TTC Phe	
GIC Val	TGC Cys	TGC Cys	AGC Ser	
CTT. Leu	GAG Glu	AAG Lys	GCC Ala	
CAT	GGC Gly	TGC	ATG Met	TAG
Ser	GGA Gly	TTG	GTA Val	GAA Glu

FIG. 39 EGFL2

SEQ ID NO: 155:

48	96	144	192
AAT	TAC	AAT	TAA
Asn	Tyr	Asn	
GTG	AGA	GAG	\mathtt{TAC}
Val	Arg	Glu	
TGT	TCA	ACT	CTC
Cys	Ser	Thr	
TTC	CCC	TGT	GAG
	Pro	Cys	Glu
ACT	AAT	AGA	GAG
Thr	Asn	Arg	
AAA Lys	TCA	GCG	GCG
GAG Glu	CTT	GGA	AAA Lys
AAG	GAC	ACT	GAA
Lys	Asp	Thr	Glu
GAG	AAA	TTC	CAA
Glu	Lys	Phe	
GCA	GTG	GGA	ACC
Ala	Val	Gly	Thr
TGT	ATG Met	CCT	CAA Gln
AAG	TTC	CAA	GTC
Lys		Gln	Val
GTC	TGC	TGC	AAA
Val		Cys	Lys
CTT	GAG	AAG	ATG
Leu	Glu	Lys	Met
CAT	GGC Gly	TGC Cys	CCC
AGC	GGA Gly	TTG	GTG Val

FIG. 40

SEQ ID NO: 156:

48		96		144		183	
AAT	Asn	TAC	$\mathrm{T} \! \mathrm{Y} \mathrm{r}$	TAC	Tyr		
	Val		Arg	AAC	Asn		
$_{\mathrm{TGT}}$	CYS		Ser	CAA	Gln		
TTC	Phe	CCC		TGC	Cys	TAA	
	\mathtt{Thr}	AAT		CGC	Arg	TAC	$\mathrm{Ty} r$
	$\text{L}\gamma$ s	TCA			Asp	CTC	Leu
GAG	Glu	CTT	Leu	$_{ m GGT}$	G1Y	GAG	Glu
3. AAG (Lys	GAC	Asp	ACT	Thr	GAG	Glu
GA(Glu	AAA	Lys	TTT	Phe	gCG	Ala
	Ala	GTG			Glu	AAA	Lys
	CYS	ATG	Met	AAT	Asn	TAC	${\rm Tyr}$
	$\text{L} \gamma$ s	TTC	Phe	CCA	Pro	TTC.	Phe
	Val	TGC	Ċys	TGC	Cys	AGC	Ser
	Leu		Glu	AAG	$\mathrm{Ly}\mathrm{s}$	CCC	Ala
	His	GGC	G1y	$^{\mathrm{TGC}}$	Cys	ATG	Met
AGC	Ser	GGA	G1Y	TTG	Leu	GTA	Val

FIG. 41 EGFL4

SEQ ID NO: 157:

AGC C Ser H	CAT His	CTT Leu	GTC Val	AA(Lys	G TGT (SCA Ala	GAG Glu	AAG Lys	GAG Glu	AAA Lys	ACT Thr	TTC Phe	TGT Cys	GTG Val	AAT Asn	48
GGA G	A GGC C	GAG G	rgc Cys	TTC .	ATG Met	GTG Val	AAA Lys	GAC Asp	CTT	TCA Ser	AAT Asn	CCC Pro	TCA	AGA Arg	TAC	96
TTG T Leu C	TGC	AAG Lys	TGC Cys	CCA Pro	AAT Asn	GAG Glu	TTT Phe	ACT Thr	\mathtt{GGT}	GGT GAT CGC Gly Asp Arg	CGC Arg	TGC	CAA	AAC Asn	TAC Tyr	144
GTA A Val M	ATG Met	GCC Ala	AGC Ser	TTC	\mathtt{TAC}	AAG Lys	CAT His	CTT	66 <i>6</i> Gly	ATT Ile	GAA	TTT Phe	ATG Met	GAG	AAA Lys	192
GCG G. Ala G	GCG GAG Ala Glu	GAG Glu	CTC	TAC	TAA	,										210

FIG. 42 EGFL5

SEQ ID NO: 158:

48	96	144	192	240	267
AAT Asn	TAC	AAT Asn	ACT Thr	TCC Ser	
GTG Val	AGA Arg	GAG Glu	TTT Phe	ACG	
TGT Cys	TCA Ser	ACT Thr	GAG Glu	AGT Ser	
TTC	CCC	TGT Cys	AAT Asn	TAC Tyr	
ACT	AAT Asn	AGA Arg	CCA	TTC Phe	
$\lambda\lambda\lambda$	TCA	GCG Ala	TGC Cys	AGC Ser	
GAG Glu	CTT	GGA Gly	AAG Lys	GCC Ala	
AAG	GAC	ACT	GAA Glu	ATG Met	TAG
GAG Glu	AAA Lys	TTC	CAA Gln	GTA Val	GAA Glu
GCA Ala	GTG Val	GGA Gly	ACC Thr	TAC Tyr	CCT
TGT Cys	ATG Met	CCT	CAA Gln	AAC Asn	CTG Leu
AAG Lys	TTC Phe	CAA Gln	GTC Val	CAA Gln	TCT Ser
GTC Val	TGC	TGC Cys	AAA Lys	TGC Cys	CTG Leu
CTT Leu	GAG Glu	AAG Lys	ATG Met	CGC Arg	TTT Phe
CAT His	GGC	TGC Cys	CCC	GAT Asp	CCC Pro
AGC Ser	GGA	TTG	GTG Val	GGT	ACT Thr

FIG. 43 EGFL6

SEQ ID NO: 159:

48	96	144	192	240	252
AAT Asn	TAC	AAT	ACT Thr	GAG Glu	
GTG Val	AGA Arg	GAG Glu	TTT Phe	GCG Ala	
${ m TGT}$	TCA Ser	ACT Thr	GAG Glu	AAA Lys	
TTC Phe	CCC	TGT Cys	AAT Asn	TAC	
ACT Thr	AAT Asn	AGA Arg	CCA	TTC	
AAA Lys	TCA Ser	GCG Ala	AAG TGC (Lys Cys)	AGC Ser	
GAG	CTT Leu	GGA Gly	AAG Lys	GCC Ala	
AAG Lys	GAC Asp	ACT Thr	GAA Glu	ATG Met	
GAG Glu	AAA Lys	TTC Phe	CAA Gln	GTÁ Val	
GCA Ala	GTG Val	GGA Gly	CAA ACC Gln Thr	TAC Tyr	
TGT	ATG Met	CCT	CAA Gln	AAC Asn	
AAG Lys	TTC Phe	CAA Gl:n	GTC Val	CAÀ G1n	
GTC Val	TGC Cys	TGC Cys	AAA Lys	TGC Cys	TAA
CAT CTT His Leu	GAG Glu	AAG Lys	ATG Met	SGC Arg	\mathtt{TAC}
	GGA GGC Gly Gly	TGC	CCC	GAT Asp	CTC
AGC Ser	GGA	TTG	GTG Val	GGT Gly	GAG Glu

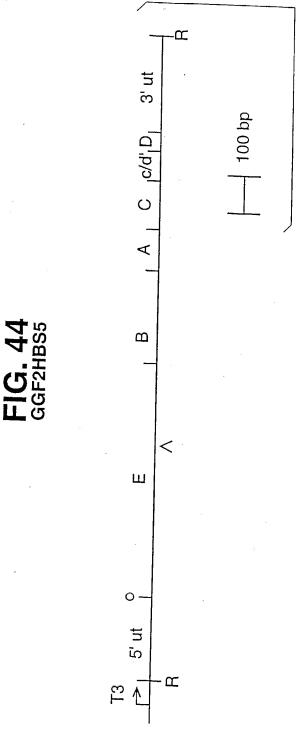


FIG. 45A Nucleotide Sequence & Deduced Acid Sequence of GGF2HBS5

SEQ ID NO: 21:	
GGAATTCCTT TTTTTTTTTTTTTTTTTTTTTTTTTT TGCCCTTATA CCTCTTCGCC	09
TITCIGIGGI ICCAICCACT ICTICCCCCI CCICCICCCA TAAACAACIC ICCIACCCCI	120
GCACCCCCAA TAAATAAATA AAAGGAGGAG GGCAAGGGGG GAGGAGGAGG AGTGGTGCTG	180
CGAGGGGAAG GAAAAGGGAG GCAGCGCGAG AAGAGCCGGG CAGAGTCCGA ACCGACAGCC	240
AGAAGCCCGC ACGCACCTCG CACC ATG AGA TGG CGA CGC GCC CCG CGC CGC	291
TCC GGG CGT CCC GGC CCC CGG GCC CCC GGC TCC GCC G	339
TCG TCG CCG CTG CTG CTG CCA CTA CTG CTG CTG CTG GGG ACC Ser Ser Pro Pro Leu Leu Pro Leu Leu Leu Leu Leu Gly Thr Val Cys Leu Leu Thr Val GGF-II 09	387
GCG GCC CTG GCG CCG GCG GCG GCC GGC AAC GAG GCG GC	435
GGG GCC TCG TGC TCG TCC CCG CCC AGC GTG GGA TCG GTG CAG G1y Ala Ser Val Cys Tyr Ser Ser Pro Pro Ser Val G1y Ser Val G1n Ala Ser Pro Val Ser Val G1y Ser Val G1n GGF-II 08	483
GAG CTA GCT CAG CGC GCG GTG GTG ATC GAG GGA AAG GTG CAC CCG Glu Leu Ala Gln Arg Ala Ala Val Val Ile Glu Gly Lys Val His Pro Glu Leu Val Gln Arg Trp Phe Val Val Ile Glu Gly Lys GGF-II 04	531

FIG. 45BNucleotide Sequence & Deduced Acid Sequence of GGF2HBS5

579	627	675	723	771	819	867	915
				,	,		
909	Ala GGC	GLY	gag Glu	GCG Ala Ala 11	CTG Leu Leu	GAG Glu	AGC Ser Gly
SCG		Ala GCC	GGC Gly	TGG Trp Trp -II	CGC Arg	AAG Lys	ACC Thr Ser
909			GCC Ala	GTG Val Val & GGF	GTG Val	CTC	AGC Ser Ser
		Pro CTC		CAG Gln Glu	ACC Thr Xaa	AGG Arg	AAC Asn Xaa
505		Pro CTG		CAC His His F-II	CTC Leu Leu	GGG Gly Tyr	GCC Ala Ala
3 AAG				GTG Val Val GGF	Sage	TGC Cys Xaa	GAC Asp Gla I 02
AGG		Arg GAG		AAG Lys Lys	TCG Ser Leu	TCC Ser Val	CCC Pro Pro Fro
		Asp GAG		GTG	GAC Asp Asp	CCC Pro Pro	GAG Glu Glu GG
				. CTG	AAG Lys	TTC Phe Phe	ATG Met Met
GCA				TYT TYR	AAG	GCC Ala Ala	TTC Phe Phe
		a Trp		CCC Pro	TTG Leu	CCC Pro Pro I 03	TTC Phe Phe
3 CAG		/ ALa 3 GGG		GCG	. G1Y	GGC CAC TO Gly His TO Gly Pro	ATC Ile Ile
3 CAG				GAG Glu	GGG 1 Gly	G17 G17 G17	TAC Tyr Tyr
990 5				GAG Glu	GCC Ala	566	AC
550 5				GGG G1y	AAA Lys Lys	ACC Thr Ala	AGC
CAG	GGC	GLY	GGG G1y	CCC	GTG Val Ala	666 61y 61y	GAC ASP

FIG. 45C Nucleotide Sequence & Deduced Acid Sequence of GGF2HBS5

36	1011	1059	1107	1155	1203	1251	1299	1347
GGC Gly	GCC Ala	GGT Gly	CTC Leu	AAA Lys	CGC Arg	GTG Val	GTG Val	GTA Val
ACG	${ m TGC}$	GCA Ala	TCT Ser	AAC Asn	CTT Leu	AAA Lys Lyx	ATC Ile	CTT
GAG	CGG	GCT	TCC Ser	AAA Lys	GAA Glu	TGC Cys Xaa	ACC Thr	CAT
CTG	AAG Lys	TCG	TAC TY <i>r</i>	CGA Arg	TĊA Ser	ATG Met Met	ATC Ile	AGC
CCT	TGC	GAA Glu	GAA Glu	AAT Asn	AAG Lys	$ ext{TAT} \\ ext{TY} \\ ext{TY}$	AAT Asn	ACA Thr
CCC Pro	CTG	CAG Gln	TCT Ser	TTG	GGG G1y	GAG Glu Glu	GCC	GGG
TTC Phe	'GTG Val	AGC Ser	AGT Ser	GAA Glu	CCA Pro	GGA Gly Gly	TCT Ser	ACT Thr
TCT Ser	CGG	AAA Lys	ACC Thr	AAT Asn	AAG Lys	TCT Ser Ser F-II	GCC	ACC
GCC Ala	AGC	ATG Met	GAA Glu	$\frac{\text{GGG}}{\text{G1}y}$	AAA Lys	GAT Asp Asp GG	AGT Ser	TCC
CGA Arg	GTC Val	GAG Glu	TGT Cys	AAT Asn	CAA Gln	GCT Ala Ala	GAC	ACA Thr
TTC Phe	GAG Glu	AAA Lys	CGG Arg Arg	AAG Lys	ATA Ile	CTG Leu Leu	AAT Asn	TCT
GCC Ala	AAG Lys	TTG Leu	A GTC CTT (1 Val Leu ? 1 Val Leu ? GGF-II 06	TTC	AAG Lys	TCA Ser Ser	GGA Gly	ACA Thr
GCC Ala	AAG Lys	CAA Gln	GTC Val Val	TGG Trp	ATC Ile	GCA Ala. Ala	TTA Leu	GCT Ala
CCG Pro	CTC Leu	CCC Pro	CTA Leu Leu	AAG Lys	AAT Asn	AAA Lys Lys	AAA Lys	AAC Asn
GCG Ala	AAC Asn	CCT	AAA Lys	TTC Phe	CAA Gln	AAC Asn	AGC	TCA
CGC Arg	CGG Arg	TTG	TCC Ser	AGA Arg	CCA Pro	ATT Ile	ATC Ile	GAA Glu

FIG. 45D

Nucleotide Sequence & Deduced Acid Sequence of GGF2HBS5

AAA TGT GCG GAG AAG GAG AAA ACT TTC TGT GTG AAT GGA GGG GAG TGC Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn Gly Gly Glu Cys	1395
TTC ATG GTG AAA GAC CTT TCA AAC CCC TCG AGA TAC TTG TGC AAG TGC Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr Leu Cys Lys Cys	1443
CCA AAT GAG TTT ACT GGT GAT CGC TGC CAA AAC TAC GTA ATG GCC AGC Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala Ser	1491
TTC TAC AGT ACG TCC ACT CCC TTT CTG TCT CTG CCT GAA Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro Glu	1530
TAGGAGCATG CTCAGTTGGT GCTGCTTTCT TGTTGCTGCA TCTCCCCTCA GATTCCACCT	1590
AGAGCTAGAT GTGTCTTACC AGATCTAATA TTGACTGCCT CTGCCTGTCG CATGAGAACA	1650
TTAACAAAAG CAATTGTATT ACTTCCTCTG TTCGCGACTA GTTGGCTCTG AGATACTAAT	1710
AGGTGTGTGA GCCTCCGGAT GTTTCTGGAA TTGATATTGA ATGATGTGAT ACAAATTGAT	1770
AGTCAATATC AAGCAGTGAA ATATGATAAT AAAGGCATTT CAAAGTCTCA CTTTTATTGA	1830
TAAAATAAAA ATCATTCTAC TGAACAGTCC ATCTTCTTTA TACAATGACC ACATCCTGAA	1890
AAGGGTGTTG CTAAGCTGTA ACCGATATGC ACTTGAAATG ATGGTAAGTT AATTTTGATT	1950
CAGAATGTGT TATTTGTCAC AAATAAACAT AATAAAAGGA AAAAAAAAA AAA	2003

FIG. 46 Schwann Cell Proliferation Assay

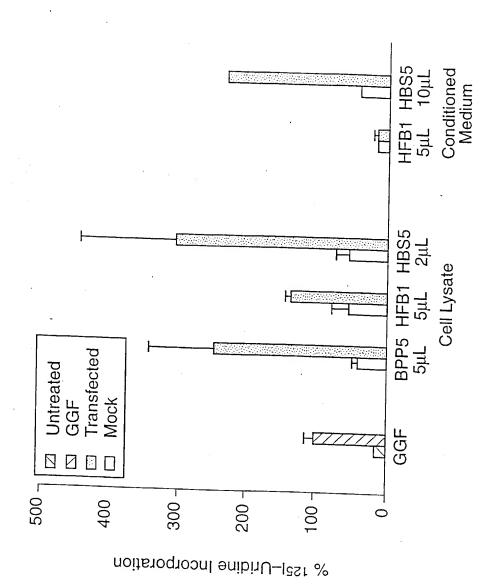
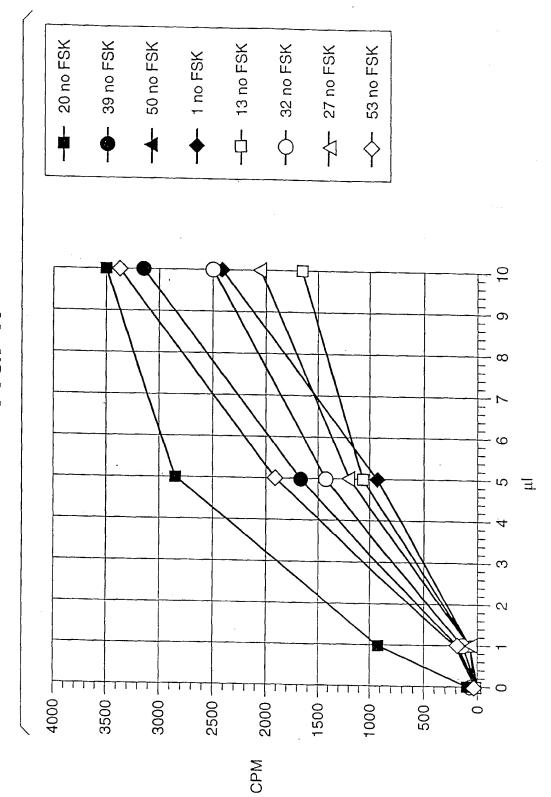


FIG. 47



CONTROLS ₽ 2 十 7 _∞ **⇔** Þ FIG. 48 Schwann Cell Assay/Baculovirus Clones μl Assayed 0.5 12000 — 14000 -10000 2000 - 0009 8000 -4000 -CPM



5-A2/3X B7 6-A2/2T AES MAXI 3 7-A2/2T AESI

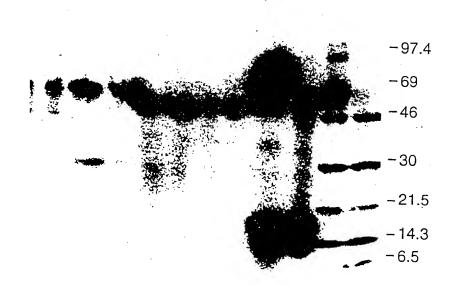
8-BV 10 25 µl

9−BV 10 6µl

11 - BV Control 6

12-CHO HBS5

13-CHO Control





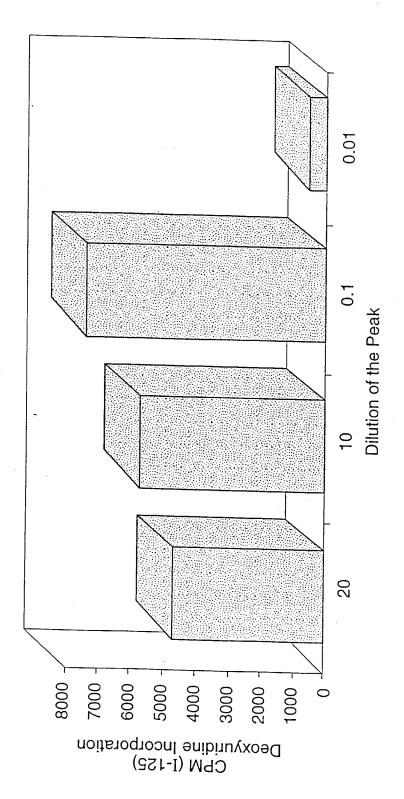
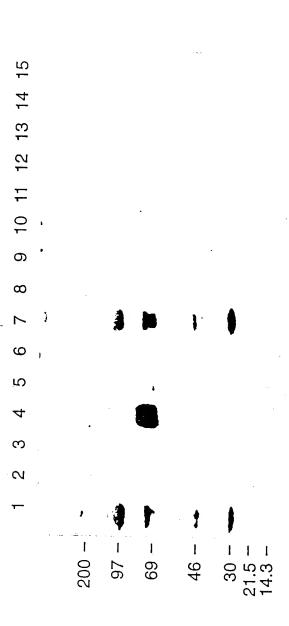
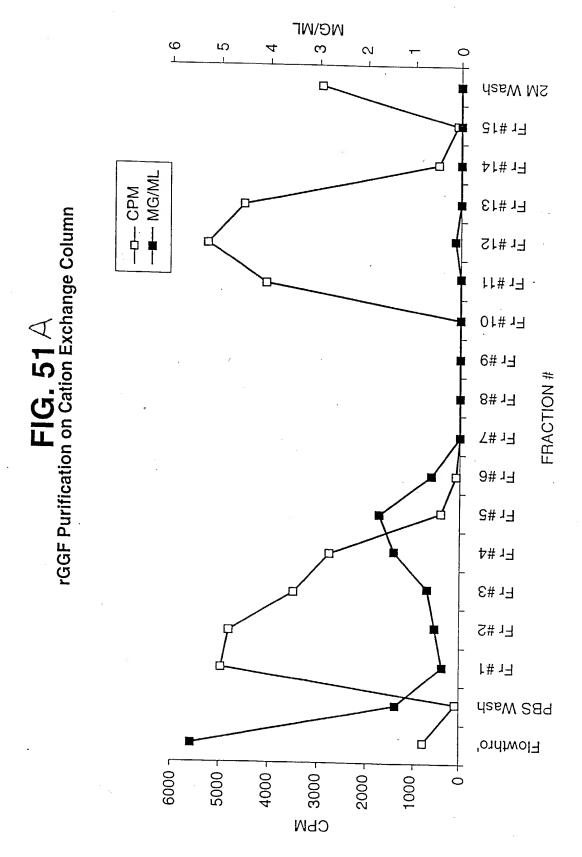


FIG. 50B





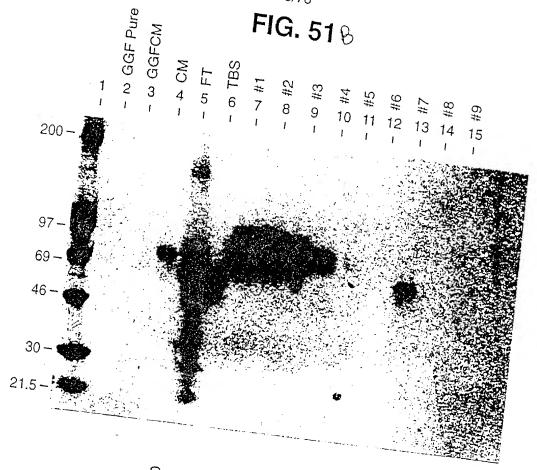
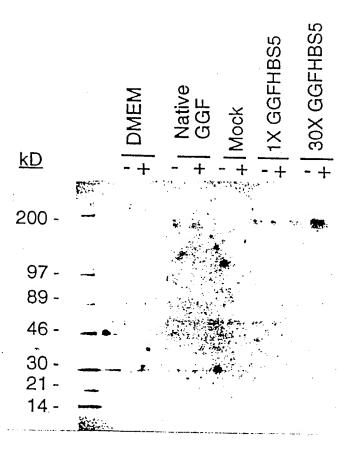


FIG. 52



1 MRMRRAPRRSGRPGPRAQRPGSAARSSPP <u>LPLLPLLLLLGTAALAPGAAG</u> NEAAPAGAS	II-8 VCYSSPPSVGSVQELAQRAAVVIEGKVHPQRRQQGALDRKAAAAAGEAGAWGGDREPPAA	II-10 GPRALGPPAEEPLLAANGTVPSWPTAPVPSAGEPGEEAPYLVKVHQVWAVKAGGLKKDSL	II-3 LTVRLGTWGHPAFPSCGRLKEDSRYIFFMEPDANSTSRAPAAFRASFPPLETGRNLKKEV O	XRCALPPQLKEMKSQESAAGSK OMSERKEGRGKGKKKERGSGKKPESAAGSQSP R K G D VP GP R V	II-6 II-18 TI-13 LVLRCETSSEYSSLRFKNFKNGNELNRKNKPQNIKIQKKPGKSELRINKASLADSGEYMC *	S R S 5 TGMPASTEGAYVSSESPIRISVSTEG	T T 6 II-15 TTGTSHLVKÇAEKEKTFÇVNGGEÇFMVKDLSNPSRYLÇKÇPNEFTGDRÇQNYVMASFYST A	LPE*
MRMRRAP	VCYSSPP	GPRALGP	LTVRLGT	SRVLCKRC.	II-6 LVLRCETS	4 KVISKLGN	TTGTSHLV	9 STPFLSLPE*
. ←	61	121	181	241 1	268 53 53	328 113 113	354 173 173	413 232 232
SEQ ID NO:170 GGFHBS5				GGFHBS5 SEQ ID NO: 171 GGFHFB1 SEQ ID NO: 172 GGFBPP5		FIG. 53	Deduced Sequences of Human & Bovine Glial Growth Factors	

FIG. 54

